Journal of Pharma Research
Available online through
www.jprinfo.com
Vol. 13 Issues 03, 2024 ISSN: 2319-5622

Original Article

DEVELOPMENT OF NOVEL SUSTAINED RELEASE ORALLY INHALABLE FORMULATION FOR EFFECTIVE TREATMENT OF RESPIRATORY DISEASES

Meda Sravani[1]*, Dr. M. Pradeep Kumar[2], B. Jagadeesh Babu[3], Manjula Challa[4]

[1]*Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Peddapalli (V) near Bhakarapeta railway station, Siddavatam (M), Kadapa, A.P India.*

[2]*Professor, Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Peddapalli (V) near Bhakarapeta railway station, Siddavatam (M), Kadapa, A.P India.*

[3]*Associate professor, Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Peddapalli (V) near Bhakarapeta railway station, Siddavatam (M), Kadapa, A.P India.*

[4]*Associate professor, Department of Pharmaceutical technology, Vasavi Institute of Pharmaceutical Sciences, Peddapalli (V) near Bhakarapeta railway station, Siddavatam (M), Kadapa, A.P India.*

Received on: 15-04-2024 **Accepted on: 26-05-2024**

ABSTRACT

Background: *Respiratory diseases require frequent dosing, affecting compliance. Innovative formulations are crucial for improved drug delivery. Inhalation therapy offers rapid action and fewer side effects. Sustained-release formulations control drug release for chronic conditions. Orally inhalable options simplify dosing, enhancing adherence. Optimizing drug release enhances treatment efficacy, benefiting patients.*

Aim: *Develop a novel sustained release orally inhalable formulation for improved treatment of respiratory diseases.*

Objective: *This study aims to develop and optimize sustained release inhalable particles for treating respiratory diseases, with a focus on improved efficacy and safety compared to existing formulations.*

Conclusion: *This study aims to develop sustained-release orally inhalable formulations for salbutamol sulphate, ambroxol hydrochloride, and montelukast sodium, crucial for respiratory diseases like asthma, allergic rhinitis, and COPD. It explores dry powder inhalers (DPIs) and various encapsulation techniques for microparticle preparation. The synthesis, characterization, and evaluation of microparticles containing the drugs, along with DPI formulations using lactohale, are detailed. The study demonstrates the microencapsulation of salbutamol sulphate with PLGA and PLGA/Eudragit RS100 at different ratios, evaluating chemical interactions, microparticle morphology, and in vitro drug release profiles.*

KEY WORDS : *Salbutamol sulphate, Ambroxol hydrochloride, Montelukast sodium |*

INTRODUCTION

Dry powder inhalers (DPIs) are devices delivering medications as dry powder to the lungs, commonly used for respiratory and systemic conditions like asthma, chronic bronchitis, and diabetes. Formulations blend drug particles (1-5 µm) with a carrier, typically lactose, enhancing dosing accuracy and flowability. Particle size (1-5 µm) ensures optimal drug deposition in the lungs, avoiding swallowing or exhalation. DPIs offer propellant-free administration, increased compliance, and stable drug delivery. They're made of polypropylene plastic, delivering measured doses via patient inhalation. Aerosolization properties depend on particle morphology, density, and composition. Production involves drug crystallization, milling, or

***Corresponding author:**
Meda Sravani
Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Peddapalli (V) Near, Bhakarapeta railway station, Siddavatam (M), Kadapa, A.P India.
Email: sravanimeda98@gmail.com
DOI: https://doi.org/10.5281/zenodo.12527984

spray drying to control particle size and distribution. Sustained DPI Formulation: Regulates lung drug delivery, reducing doses and side effects. Useful for respiratory diseases and systemic therapy. Microencapsulation Methods: Spray drying, congealing, evaporation, diffusion, coacervation, and air coating. Lyophilization: Dehydrates pharmaceuticals for DPIs. Respiratory System: Enables gas exchange, controlled by diaphragm and ribs.Infection: Enters via respiratory, oral, or urogenital tracts, countered by mucous membranes and antibodies. Asthma: Chronic lung inflammation, triggered by various factors.Allergic Rhinitis: Nasal inflammation due to allergens, causing typical symptoms.COPD: Lung disorders, including chronic bronchitis and emphysema, often caused by smoking. Inhaler: Portable device for respiratory drug delivery, including DPIs, aerosol inhalers, nebulizers, and nasal inhalers.DPI: Delivers dry powder medications like salbutamol and fluticasone. Examples: Rotahaler, diskus, aerolizer. Antiasthma Drugs: Sustained-release formulations enhance lung drug delivery. Includes Salbutamol sulphate, Ambroxol hydrochloride, Montelukast sodium.Polymers: Sustained-release PLGA (50:50) and PLGA (75:25) maintain constant drug levels, soluble in organic solvents.

MATERIALS AND METHODS

Methods:

Chemical Reagents:

Salbutamol Sulphate (SS) and Ambroxol hydrochloride (AH) from Fourrts Laboratories Pvt Ltd, Chennai.Montelukast Sodium (MS), polyvinyl alcohol, and hard empty gelatin capsules (size 3) from Orchid Pharmaceuticals, Chennai.Dichloromethane, Methanol, and Acetonitrile from Qualigens, Mumbai.PLGA (50:50) and PLGA (75:25) from Birmingham Polymer Inc, USA.Eudragit RS 100 from Evonik India Pvt Ltd.Potassium dihydrogen orthophosphate, Sodium chloride, and Sodium hydroxide from SD-fine chemicals, Mumbai, India.Dialysis membrane (14kDa molecular weight) from Himedia, Mumbai.Bright-line hemocytometer, cover slip (Hausser Scientific, Horsham, PA), 70% (v/v) ethanol, Microscope (100× magnification), and Micropipette (15 µL samples) from Orange Progene Pvt Ltd., Chennai.Purified water obtained by reverse osmosis (Kens).All materials used were of analytical grade.

Instrumentation Used:

High-resolution UV-Visible double-beam spectrophotometer V760 by Jasco: Used for estimating drug content. FTIR Spectrometer Perkin Elmer 2000: Utilized for drug-polymer interaction analysis, with a scanning range of 400-4000 cm^-1. SEM (Scanning Electron Microscope) VEGA3 LMU by TESCAN: Employed for investigating the surface appearance and shape of the drug-polymer complex. Sympatec Helos Rodos: Utilized for particle size analysis. Anderson Cascade Impactor (ACI) by Copley Scientific, equipped with a critical flow controller TPK 2000: Used for in vitro deposition studies.

Micro particle Synthesis:

Solvent Evaporation Method: Involves preparing an oil-in-water (o/w) emulsion with a polymer dissolved in dichloromethane (DCM) as the organic phase. The drug solution (SS/AH/MS) is added to this mixture and sonicated using a probe sonicator to form the emulsion. This emulsion is then dropwise injected into an aqueous phase containing 2% w/v polyvinyl alcohol (PVA). Emulsification is achieved by homogenization at 10,000 rpm for 10 minutes using a homogenizer (Viritis Cyclone IQ, USA). The resulting emulsion is stirred for 12 hours at 25±2°C using a magnetic stirrer until dichloromethane is completely removed. The microparticles are then recovered by centrifugation (15,000 rpm, 20 minutes, 4°C). **Washing and Recovery**: The precipitate is thoroughly washed to remove PVA. The product is dispersed in cold water and recovered by lyophilization. **Batch Variation**: Different batches of microparticles are prepared by maintaining an organic phase to aqueous phase ratio of 1:5 to ensure yield, while varying the drug to polymer ratios.

Drug Content Determination:

Equipment Used: High resolution UV-Visible double beam spectrophotometer.

Procedure:

• Pure drug (1mg) transferred into a 100 ml volumetric flask.

• Added 10 ml of phosphate-buffered saline (PBS; pH 7.4) and dissolved.

• Added 90 ml of purified water and sonicated for 15 minutes with intermittent shaking for complete dispersion.

• Similar procedure adopted for different drug quantities to create a standard calibration graph.

Calculation:

Drug content in microparticles calculated using the formula:

Amount of the Drug = (Asam × Cstd) / Astd

where:

Asam = absorbance of the sample solution,

Cstd = concentration of the drug in standard solution,

Astd = absorbance of standard drug solution.

Percentage Yield

The percentage yield was caluculated by using the following formula.

Percentage yield = (Total weight of microparticles / Total weight of drug and polymers) × 100

Entrapment Efficiency

For 10mg of the microparticle, 15mL acetonitrile and 30mLof sodium hydroxide were used for extraction. The mixture was filtered through a 0.45µm membrane, after dilutions with 70mL of purified water; the drug content was measured using purified water as a blank.

Formula:

Entrapment efficiency = (Percentage of drug content estimated / Percentage of drug content theoretical) × 100

Particle Size Determination:

Method: Laser diffraction using the HELOS particle size analyzer.

Sample Amount: 100 mg of powder.

Particle Size Representation: D0.5.

Dry Powder Inhaler (DPI) Preparation:

Method: Dispersion of inhalable lactose with drug-based microparticles.

Carrier: Inhalable lactose (Lactohale 100) with particle size of 5-10 µm fraction.

Drug Amount: 1 mg of drug equivalent mixed with lactohale to maintain weight at 20 mg.

Capsule: Inhalable hard empty gelatin capsules (Size 3) stored in airtight HDPE containers.

Fill Weight: 20 mg per capsule containing 1 mg of drug equivalent microparticles.

Weight Variation

Weight variation was calculated for 20 filled capsules. Each capsule content was removed, empty capsule weight was noted and subtracted from the gross weight of the capsule with content (Murthyet al.2010).

20 Capsules content in mg

$$\text{Average fill weight (mg)} = \frac{\text{20 Capsules content in mg}}{20}$$

Drug Content UV:
Extraction: Drug extracted from DPI capsules using 0.1 M sodium hydroxide after dissolving capsules in acetonitrile.

Procedure: 25 mL acetonitrile used to dissolve capsules, followed by extraction with 30 mL sodium hydroxide for 10 capsules.

Filtration: Mixture filtered through a 0.45 µm membrane.

Measurement: Drug content measured in UV-VIS spectrophotometer after dilution with 70 mL purified water, using purified water as blank.

In Vitro Drug Release Study:

Method: Dialysis bag diffusion method used for in vitro dissolution evaluation.

Medium: Phosphate-buffered saline (PBS) at pH 7.4 used as diffusion medium.

Membrane: Dialysis membrane with 14 kDa molecular weight cutoff employed.

Procedure: Aqueous dispersion equivalent to 10 mg of drug equivalent dry powder placed in a sealed dialysis bag.

Immersion: Dialysis bag immersed in 250 ml of diffusion medium and stirred at 100 rpm.

Sampling: Samples withdrawn at predetermined intervals, with the receptor phase replenished with an equal volume of blank after each withdrawal.

Analysis: Samples filtered through 0.46 µm filter, diluted with PBS pH 7.4, and absorbance measured using UV/Vis spectrophotometry.

Data Analysis: Cumulative percent drug calculated and plotted against time. Experiments conducted in triplicates.

RESULTS AND DISCUSSION

The microparticles were prepared using a combination of PLGA (50:50), PLGA (75:25), and Eudragit RS100. Various batches were made with different ratios of organic phase to aqueous phase (OP: AP::1:5) to maintain yield. The formulations for Salbutamol: PLGA (50:50) microparticles are summarized in

Formulation Code	SS:PLGA 50:50	Salbutamol Sulphate (mg)	PLGA 50:50 (mg)	Volume of DCM (ml) - OP	AP Volume (2% PVA) (ml)
K1	1:1	50	50	5	25
K2	1:2	50	100	5	25
K3	1:3	50	150	5	25
K4	1:4	50	200	5	25

(OP: Organic phase, AP: Aqueous phase)

The formulation details for Salbutamol:PLGA (75:25) microparticles are as follows:

Formulation Code	SS:PLGA 75:25	Salbutamol Sulphate (mg)	PLGA 75:25 (mg)	Volume of DCM (ml) - OP	AP Volume (2% PVA) (ml)
L1	1:1	50	50	5	25
L2	1:2	50	100	5	25
L4	1:4	50	200	5	25

(OP: Organic phase, AP: Aqueous phase)

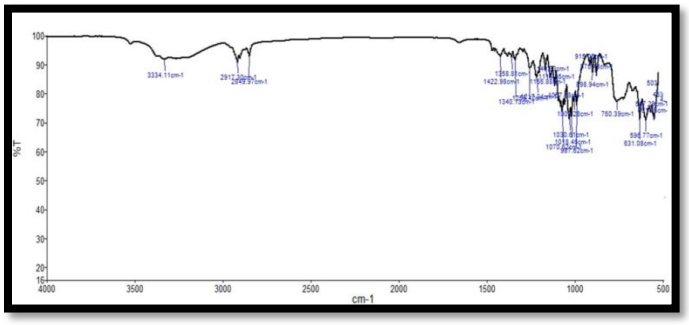
The formulation details for Salbutamol:Eudragit RS100 microparticles:

Formulation Code	SS:Eudragit RS100	Salbutamol Sulphate (mg)	Eudragit RS100 (mg)	Volume of DCM (ml) - OP	AP Volume (2% PVA) (ml)
M1	1:1	50	50	5	25
M2	1:2	50	100	5	25
M4	1:4	50	200	5	25

(OP: Organic phase, AP: Aqueous phase)

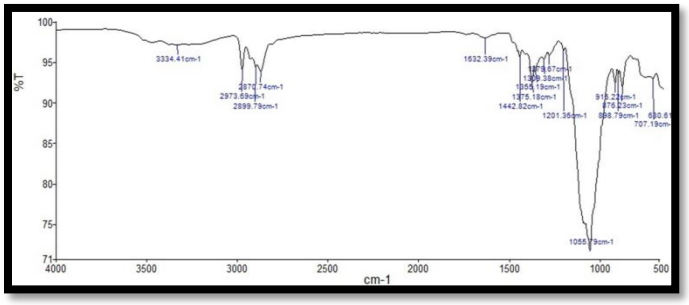
EVALUATION

Fourier Transform Infrared Spectroscopy (FTIR)



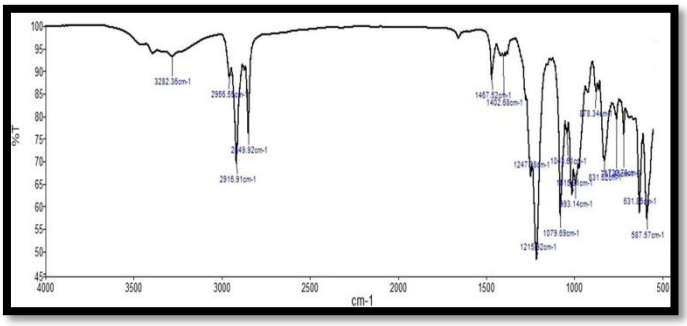
Fourier Transform Infrared Spectragraph of PLGA (50:50)

FT-IR analysis of PLGA (50:50) revealed peaks indicating C=O stretching at 3334 cm-1, CH stretching at 2917 cm-1 and 2849 cm-1, and sharp bands representing C-C vibrations at approximately 1422 cm-1, 1358 cm-1, 1340 cm-1, and 1030 cm-1.



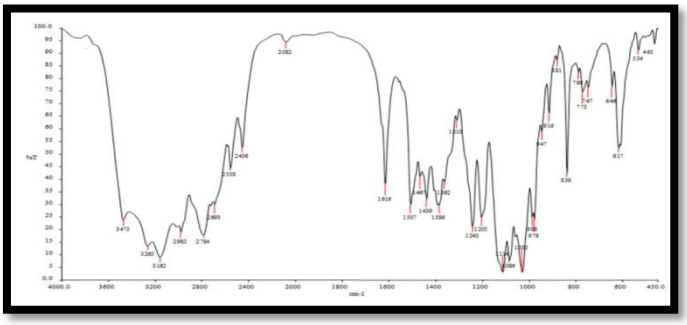
Fourier Transform Infrared Spectragraph of PLGA (75:25)

FT-IR analysis of PLGA (75:25) exhibited peaks indicating C=O stretching at 3334 cm-1, CH stretching at 2973 cm-1 and 2899 cm-1, and sharp bands representing C-C vibrations at approximately 1632 cm-1, 1442 cm-1, 1375 cm-1, and 1355 cm-1. Another stretching peak suggested the presence of carbon groups.



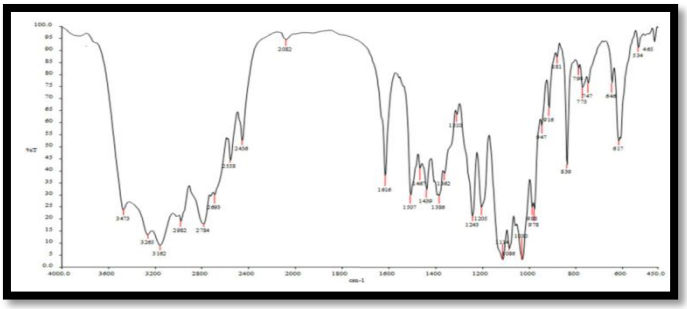
Fourier Transform Infrared Spectra graph of Eudragit RS 100

FT-IR analysis of Eudragit RS100 revealed peaks indicating C=O stretching at 3282 cm-1, CH stretching at 2956 cm-1 and 2916 cm-1, and a peak related to N-CH stretching at 2149 cm-1. Sharp bands observed at approximately 1457 cm-1, 1402 cm-1, 1247 cm-1, 1215 cm-1, and 1079 cm-1 indicate C-C vibrations.



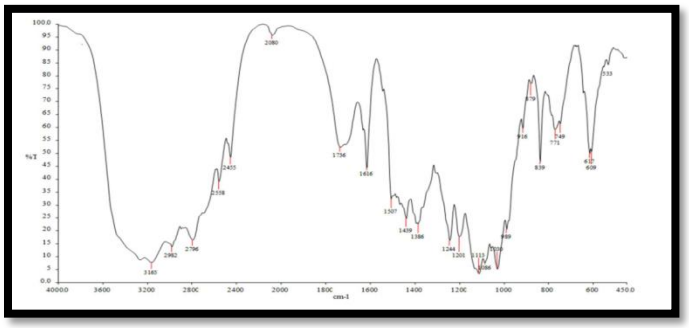
Fourier Transform Infrared Spectra graph of salbutamol sulphate

FT-IR analysis of Salbutamol Sulphate (SS) showed peaks indicating C-H stretching at 3473 cm-1 and 3265 cm-1, NH and CH stretching at 3162 cm-1 and 2982 cm-1 respectively. Peaks corresponding to hydroxyl groups were observed at 2558 cm-1, 2456 cm-1, and 2082 cm-1. Sharp bands observed at approximately 1616 cm-1, 1507 cm-1, 1205 cm-1, 1114 cm-1, 1086 cm-1, and 1030 cm-1 indicate C-C vibrations.



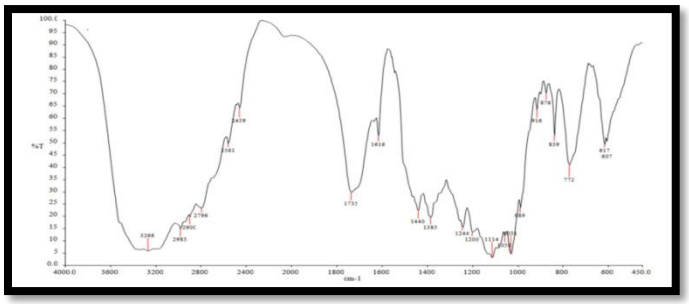
Fourier Transform Infrared Spectragraph of SS : PLGA (50:50) microparticles

FTIR spectra of Salbutamol Sulphate (SS): PLGA (50:50) microparticles showed peaks corresponding to pure SS, indicating stability with no observed chemical interaction between SS and the microparticles.



Fourier Transform Infrared Spectra graph SS: PLGA (75:25) microparticles

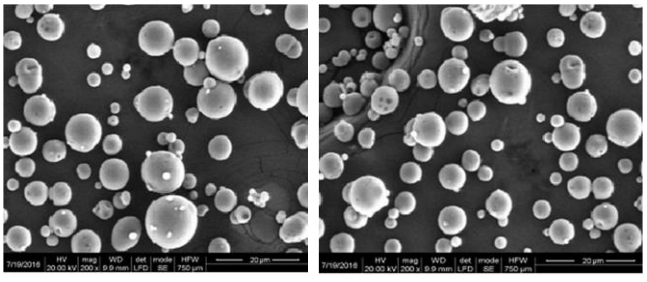
The SS: PLGA 75:25 microparticles exhibited peaks with slight variations, yet maintaining the same stretching patterns as pure SS. This confirms the stability and compatibility of the microparticles.



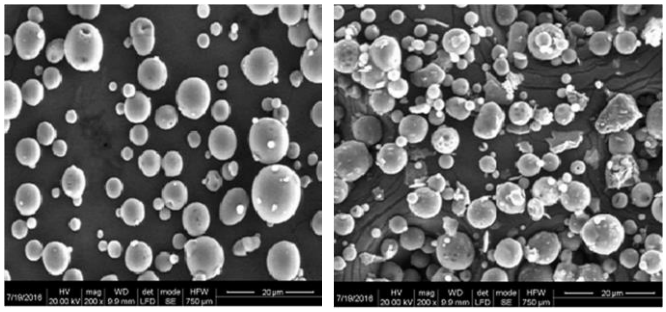
Fourier Transform Infrared Spectragraph of SS: Eudragit RS100 microparticles

The peaks observed in the spectra of Salbutamol Sulphate (SS) and Eudragit RS100 microparticles showed no difference in the positions of absorption bands, indicating no chemical interaction between the drug and polymer in the solid state.

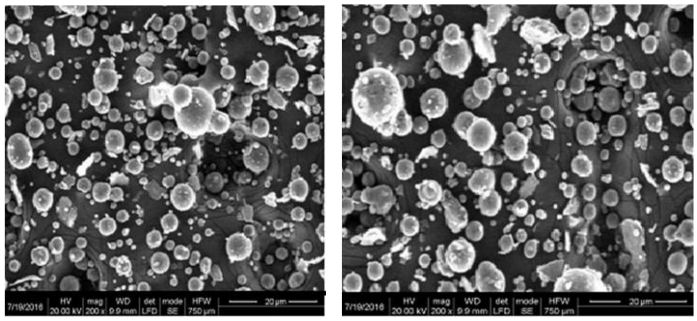
Scanning Electron Microscopy (SEM)



Scanning electron microscope photograph of SS: PLGA (50:50) of 1:1 ratio



Scanning electron microscope photograph of SS:PLGA (75:25) of 1:1 ratio



Scanning electron microscope photograph of SS:Eudragit RS 100 of 1:1 ratio

Particle Size Determination

The particle size of microparticles varied across different drug: polymer ratios, as detailed in Tables 3.4 - 3.6. Generally, an increase in the proportion of polymers led to larger particle sizes across all formulations. Specifically, formulations with a drug: polymer ratio of 1:1 exhibited smaller particle sizes compared to ratios such as 1:2, 1:3, and 1:4.

Mean particle size of micro particles (SS: PLGA(50:50))

Formulation Code	Drug: Polymer	Particle size (D0.5 µm) Mean ± SD
K1	1:1	1.74 ± 0.6
K2	1:2	4.69 ± 0.7
K3	1:3	4.86 ± 0.4
K4	1:4	4.79 ± 0.3

Mean particle size of microparticles (SS:PLGA (75:25)

Formulation Code	Drug: Polymer	Particle size (D0.5 µm) Mean ± SD
L1	1:1	1.80 ± 0.2
L2	1:2	5.15 ± 0.5
L4	1:4	5.19 ± 0.2

Mean particle size of microparticles (SS: Eudragit RS 100)

Formulation Code	Drug: Polymer	Particle size (D0.5 µm) Mean ± SD
M1	1:1	1.86 ± 0.8
M2	1:2	4.98 ± 0.6
M4	1:4	5.11 ± 0.4

Percentage Yield and Entrapment Efficiency

The salbutamol content of microparticles was analyzed using a UV-VIS spectrophotometer at 278 nm to determine percentage yield and entrapment efficiency. Results were provided in Tables 3.7 - 3.9. Percentage yield was calculated as the ratio of actual microsphere weight to initial materials used, with values consistently above 70%. Entrapment efficiency, calculated as the ratio of estimated to theoretical drug content, remained above 68% for all trials. Slight variations in both parameters across formulations may be attributed to increased polymer concentrations.

Entrapment efficiency and % yield of microparticles (SS: PLGA (50:50))

Formulation Code	Drug: Polymer	Entrapment efficiency (%) Mean ± SD	% Yield Mean ± SD
K1	1:1	76.62 ± 0.32	82.25 ± 1.38
K2	1:2	76.50 ± 0.04	80.23 ± 2.12
K3	1:3	76.30 ± 1.20	79.34 ± 1.97
K4	1:4	75.60 ± 1.84	79.12 ± 2.06

Entrapment efficiency and % yield of microparticles (SS: PLGA (75:25)

Formulation Code	Drug: Polymer	Entrapment Efficiency (%) Mean ± SD	% Yield Mean ± SD
L1	1:1	73.12 ± 0.41	80.12 ± 1.01
L2	1:2	72.91 ± 0.12	79.12 ± 1.72
L4	1:4	71.02 ± 1.24	77.14 ± 1.74

Entrapment efficiency and % yield of micro particles (SS: Eudragit RS100)

Formulation Code	Drug: Polymer	Entrapment Efficiency (%) Mean ± SD	% Yield Mean ± SD
M1	1:1	71.16 ± 0.54	75.21 ± 1.72
M2	1:2	70.82 ± 0.14	73.62 ± 1.82
M4	1:4	68.06 ± 1.16	70.24 ± 1.94

DRY POWDER INHALER PREPARATION

Micro particles were physically mixed with coarse carrier lactose, specifically inhalable grade lactohale, to improve aerosol properties for the creation of respirable sustained release dry powder inhaler (DPI) formulations. This approach was detailed in studies by Hamishehkar et al. (2010), Hassan & Lau (2011), and Ravindra et al. (2009).

Evaluation of DPI Capsule

Weight variation and drug content for DPI formulations were evaluated by individually weighing filled capsules after removing their contents. Weight variation was determined by subtracting the weight of the empty capsule from the gross weight of the capsule plus contents. Drug content was assessed using a UV-Vis spectrophotometer at 278 nm. This assessment method was documented by Marie et al. (2004), Newman & Busse (2002), Niti Yadav & Alka Lohani (2013), and Guchardi et al. (2008).

Weight variation and drug content of DPI capsules (SS: PLGA (50:50))

Formulation Code	Weight Variation (mg ± SD)	Drug Content (%) Range
K1	20.06 ± 0.05	99.2-100.5
K2	20.03 ± 0.12	99.5-102.5
K3	20.15 ± 0.20	98.5-101.1
K4	20.09 ± 0.17	99.9-100.8

Weight variation and drug content of DPI capsules (SS: PLGA (75:25))

Formulation Code	Weight Variation (mg ± SD)	Drug Content (%) Range
L1	20.11 ± 0.12	99.0-101.4
L2	19.93 ± 0.02	99.1-101.5
L4	20.09 ± 0.17	98.7-100.7

Weight variation and drug content of DPI capsules (SS: Eudragit RS10

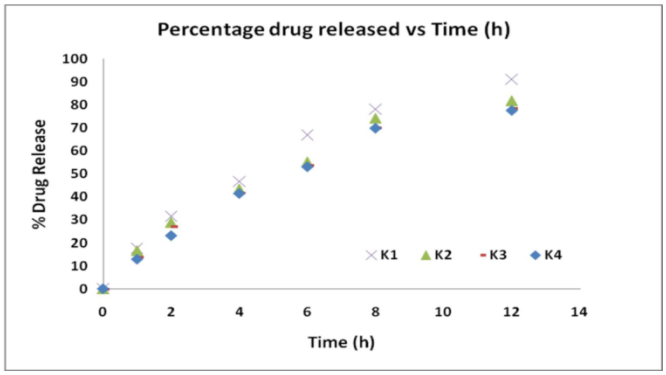
Formulation Code	Weight Variation (mg ± SD)	Drug Content (%) Range
M1	19.94 ± 0.20	98.9-102.5
M2	20.01 ± 0.14	98.7-102.7
M4	20.12 ± 0.20	99.4-100.8

IN VITRO DRUG RELEASE STUDY

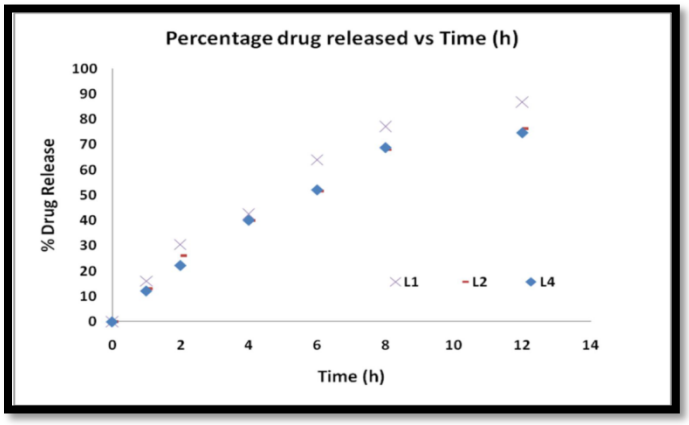
The in vitro dissolution of salbutamol sulfate (SS) from DPI formulations was analyzed using a dialysis bag diffusion method. Aqueous dispersions equivalent to 10 mg of SS from each DPI formulation were placed in dialysis bags and immersed in Phosphate Buffered Saline (PBS) at pH 7.4. Samples were withdrawn at predetermined intervals, filtered, and analyzed using a UV-Vis spectrophotometer. The experiments were conducted in triplicate at 37°C. The percentage of drug released at 12 hours for various formulations was: K1 (91.23%), K2 (81.92%), K3 (78.42%), K4 (77.71%), L1 (86.92%), L2 (76.42%),

L4 (74.61%), M1 (85.05%), M2 (75.41%), and M4 (73.24%). All formulations exhibited drug release of not less than 77% at 12 hours. K1 (SS: PLGA 50:50), L1 (SS: PLGA 75:25), and M1 (SS: Eudragit RS100) demonstrated the highest drug release percentages. K1's higher dissolution may be attributed to its internal structure, where PLGA 50:50 with surface pores influences dissolution by increasing polymer concentration and rigidity. Consequently, the 1:1 drug-polymer ratio exhibited superior dissolution compared to 1:2 and 1:4 ratios.

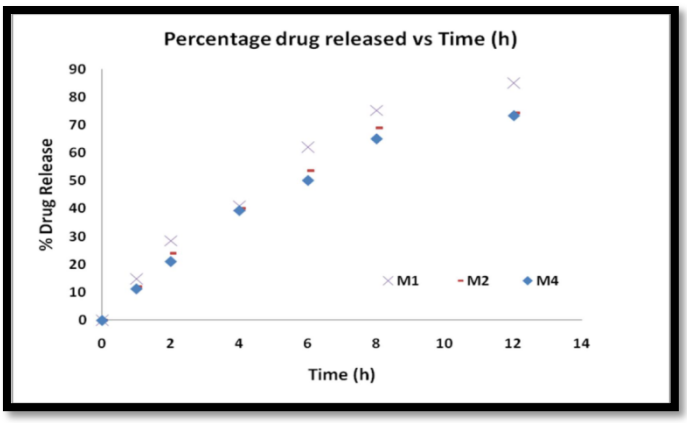
Comparative evaluation of drug release percentages between formulations with different drug-to-polymer ratios (1:1, 1:2, and 1:4) revealed that PLGA(50:50) exhibited superior dissolution profiles due to higher dissolution rates. Specifically, formulations K1, L1, and M1 (1:1 ratio) demonstrated enhanced drug release compared to formulations with higher polymer concentrations (K2, L2, M2, K4, L4, and M4). This suggests that the internal structure of PLGA(50:50), characterized by increased polymer concentration and surface pores, contributed to the improved dissolution profile observed.



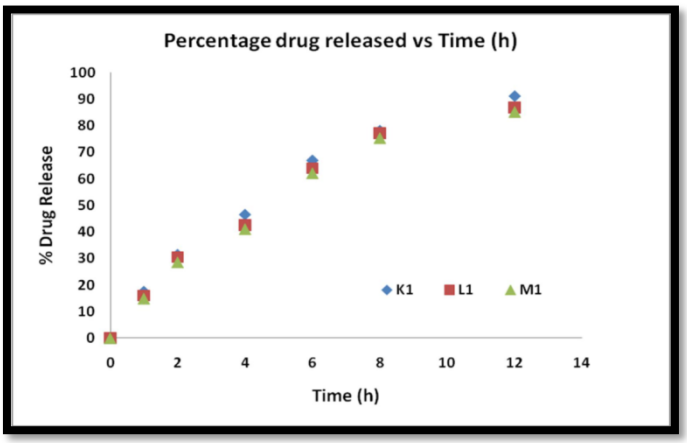
Cumulative Percent drug release versus time (h) for TrialsK1-K4



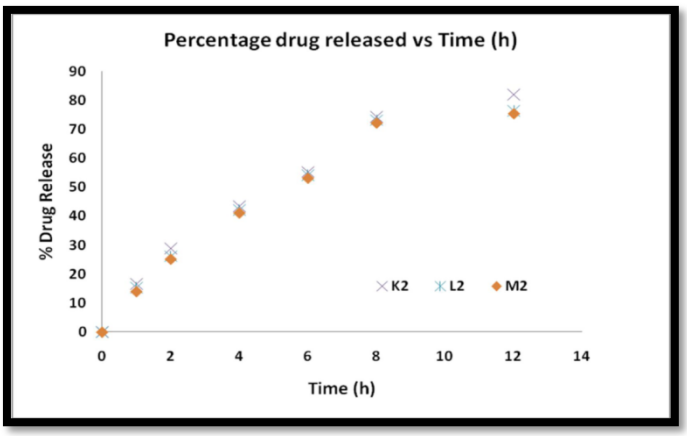
Cumulative Percent drug release versus time (h) for TrialsL1-L4



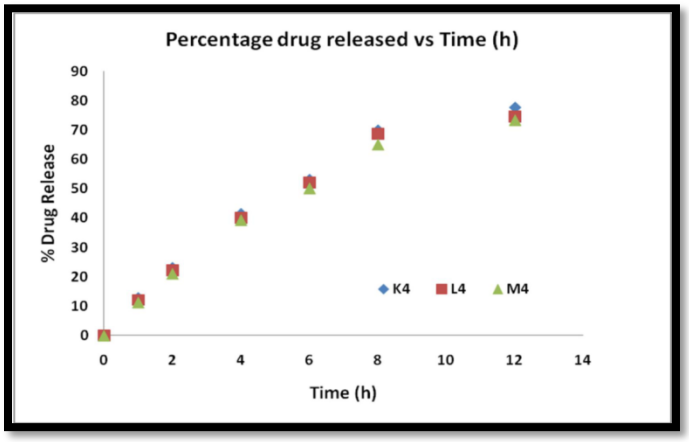
Cumulative Percent drug release versus time (h) for Trials M1-M4



Cumulative Percent drug release versus time (h) for Trials K1-M1



Cumulative Percent drug release versus time (h) for TrialsK2-M2



Cumulative Percent drug release versus time (h) for TrialsK4-M4

SUMMARY AND CONCLUSION

This study focuses on developing sustained-release orally inhalable formulations for three respiratory drugs: salbutamol sulphate, ambroxol hydrochloride, and montelukast sodium.

Chapter 1: Provides an overview of dry powder inhalers (DPIs), their manufacturing methods, and the significance of respiratory diseases like asthma, allergic rhinitis, and chronic obstructive pulmonary disease (COPD). Various encapsulation techniques for microparticle preparation and their applications in drug delivery are discussed.

Chapter 2: Covers the synthesis of microparticles containing the aforementioned drugs, along with procedures for calculating drug content, percentage yield, and entrapment efficiency. It also details the preparation of DPI formulations using lactohale, including their characteristics and in vitro/in vivo studies.

Chapter 3: Demonstrates the microencapsulation of salbutamol sulphate with PLGA (50:50) and PLGA (75:25) / Eudragit RS100 at various ratios. The microparticles are combined with lactohale to create DPI formulations. Chemical interactions, microparticle morphology, and in vitro drug release profiles are evaluated.

Future Directions: The study opens avenues for clinical research aimed at effectively treating respiratory diseases with sustained-release orally inhalable dry powder formulations. The ease of administration and compatibility of DPI formulations offer promising prospects for respiratory treatment, benefitting both physicians and patients.

REFERENCES

1. Agertoft,L & Pederson, S 2003, 'Lung deposition and systemic availability of fluticasone diskus and budesonide turbuhaler in children',American Journal ofrespiratory criticalcare Med.vol.168, pp.779-782.

2. Aliasgar Kundawala, VishnuPatel, Harsha Patel & Dhaglaram Choudhary 2014,' Preparation, In Vitro Characterization, and In Vivo Pharmacokinetic Evaluation of Respirable Porous Microparticles Containing Rifampicin', Sci Pharm, vol. 82, no. 3, pp. 665-681.

3. Ali Ahmed Yas Al-Jipour 2014, 'Preparation and Evaluation of Inhalable Sustained Release Sildenafil Citrate Solid Lipid Micro particles Dispersions', Global Journal of Medical Research: Drug Discovery, Toxicology and Medicine, vol. 14, no. 5, pp. 1-7.

4. Ana Grenha, Bego na Seijo & Carmen Remunan-Lopez 2005, 'Microencapsulated chitosan nano particles for lung protein delivery', European Journal of Pharmaceutical Sciences, vol. 25, pp. 427-437

5. Antoine, M, Helene Boireau, Maria Joao Horta & Rita Vanbever 2008, 'Optimization of the aerosolization properties of an inhalation dry powder based on selection of excipients', European Journal of Pharmaceutics and Biopharmaceutics, vol. 70, pp. 839-844.

6. Austin, V & Warren H Finlay 2002, 'Deagglomeration of dry powder pharmaceutical Aerosols', International Journal of Pharmaceutics., vol. 248, pp. 39-50

7. Bennett, WD, Brown, JS, Zeman, KL, Hu, SC, Scheuch, G & Sommerer, K 2002,'Targeting delivery of aerosols to different lung regions', J Aerosol Med, vol. 15, no. 2, pp. 179-188.

8. Bonev, B, Hopper, J & Parisot, J 2008, 'Principles of assessing bacterial susceptibility to antibiotics using the agar diffusion method', J.Antimicrob.Chemother.vol.61,pp.1-7.

9. Carola Buccellati, Francesca Fumagalli, Serena Viappiani & Giancarlo Folco. 2002, Leukotriene modifiers: novel therapeutic opportunities in asthma, Il Farmaco., vol. 57, pp. 235-242.

10. Chan, HK 2006, 'Dry powder aerosol delivery systems: current and future research Directions', J Aerosol Med, vol. 19, no. 21-27.

11. Chan, HK 2006, 'Dry powder aerosol drug delivery opportunities for colloid and surface scientists', Colloids and Surfaces A: Physicochemical and Engineering Aspects, vol. 284, pp. 50-55.

12. Claudius Weiler, Markus Wolkenhauer, Michael Trunk & Peter Langguth 2010, 'New model describing the total dispersion of dry powder agglomerates', Powder Technology, vol. 203, pp. 248-253.

13. Coates, MS, Fletcher, DF, Chan, HK & Raper, JA 2005, 'The role of capsule on the performance of a dry powder inhaler using computational and experimental analyses', Pharmaceutical research. vol. 22, no. 6, pp. 923-932.

14. Cook, RO, Pannu, RK &Kellaway, IW 2005, 'Novel sustained release microspheres for pulmonary drug delivery', J Control Release. vol. 104, pp. 79-90.

15. Corrigan, DO, Healy, AM & Corrigan, OI 2006, 'Preparation and release of salbutamol from chitosan and chitosan co-spray dried compacts and multi particulates', Eur JPharm Biopharm. vol.62, pp. 295-305.

16. Currie, GP & Mclaughlin, K 2006, 'The expanding role of leukotriene receptor antagonists in chronic asthma', Ann Allergy Asthma Immunol. Vol.97, pp.731–41.

17. Cynthia, B, Catherine lombry, Veronique preat& Rita vanbever. (2001), 'Comparison ofparticle sizing techniques in the case of inhalation dry powders', Journal of pharmaceutical sciences, vol. 90, no. 12, pp. 2032-41.

18. de Boer, AH, Gjaltema, D, Hagedoorn, P & Frijlink, HW 2002, 'Characterization of inhalation aerosols: a critical evaluation of cascade impactor analysis and laser diffraction technique', International Journal of Pharmaceutics, vol. 249. pp. 219-231.

19. De Boer, AH, Hagedoorn, P, Westerman, EM, Le Brun, PPH, Heijerman, HGM & Frijlink, HW 2006, 'Design and in vitro performance of a disposable inhaler with multiple air classifier technology for high powder doses',Eur.J.Pharm.Sci.vol.28,pp.171-178.

20. Delvadia, R, Hindle, M, Longest, PW & Byron, PR 2012, 'In vitro tests foraerosol deposition II: IVIVCs for different dry powder inhalers in normal adults',J Aerosol Med Pulm Drug Deliv, vol.26, pp.138-44.

21. Delvadia, R, Longest, PW & Byron, PR 2012, 'In vitro tests for aerosol deposition. I. scaling a physical model of the upper airways to predict drug deposition variation in normal humans', Aerosol Med Pulm Drug Deliv. Vol. 25, pp.32-40.

22. Derek, ID & Jesse Zhu 2008, 'Dry powder platform for pulmonary drug delivery', Particuology. vol. 6, pp. 225-238.

23. Ertunc, O, Koksoya, C, Wachtelc, H & Delgadoa, A 2011, 'A method for the aerodynamic design of dry powder inhalers', International Journal of Pharmaceutics, vol. 416, pp. 25-34.

24. Frijlink, HW& de Boer, AH2004, 'Dry powder inhalers for pulmonary drug delivery', Expert opinion drug delivery, vol.1, pp.67-86.

25. Gabrielle, P & Karim, A 2010, 'Formulation strategy and use of excipients in pulmonary drug delivery', International Journal of Pharmaceutics, vol. 392, pp. 1-19.

26. Gabrielle, P, Francis Vanderbist & Karim Amighia 2008, 'Correlations between cascade impactor analysis and laser diffraction techniques for the determination of the particle size of aerosolised powder formulations' ,International Journal of Pharmaceutics , vol.358, pp.75-81.

27. Groneberg, DA, Witt, C, Wagner, U, Chung, KF & Fischer, A 2003, 'Fundamentals of pulmonary drug delivery', Respiratory Medicine.vol. 97, pp. 382-387.

28. Guchardi, R,Frei, M,John, E &Kaerger, JS 2008, 'Influence of fine lactose and magnesium Stearate on low dose dry powder inhaler formulations', International Journal of Pharmaceutics. vol. 348, pp.10-17.

29. Guchardi, R, Frei, M, John, E &Kaerger, JS 2008, 'Influence of fine lactose and magnesium stearate on low dose dry powder inhaler formulations', Int. J. Pharm, vol. 348,pp. 10-17.

30. Hak Kim Chan & Nora YK Chew 2003, 'Novel alternative methodsfor the delivery of drugs for the treatment of asthma', Advanced Drug Delivery Reviews. vol. 55, pp. 793-805.

How to cite this article:

Meda Sravani*, DEVELOPMENT OF NOVEL SUSTAINED RELEASE ORALLY INHALABLE FORMULATION FOR EFFECTIVE TREATMENT OF RESPIRATORY DISEASES J Pharma Res, 2024; 13(03): 31-39.
DOI: https://doi.org/10.5281/zenodo.12527984

Conflict of interest: The authors have declared that no conflict of interest exists.
Source of support: Nil

