Available online at *www.ujpronline.com*
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

RESEARCH ARTICLE

FORMULATION AND EVALUATION OF FAST DISSOLVING HERBAL FILM CONTAINING RESERPINE FOR THE MANAGEMENT OF PULMONARY ARTERIAL HYPERTENSION

Said Salim Said[1,3], Nabisere Zulfa[1], Gokul Bhimajiyan[1], Chukwuma J. Okafor[2], Burhani Simai[3], Sabra Salim Rashid[4], Abbas S. Ibrahim[5], Ahmad Makame Mwadini[3], Harshil Majethia[1], Prasanna Kumar Desu[1], Haji Juma Hamisi[3]

[1]*Department of Pharmaceutical Science, Marwadi University, Rajkot, Gujarat, India.*
[2]*Department of Pathology and Biochemistry, State University of Zanzibar, Tanzania.*
[3]*Zanzibar Food and Drug Agency (ZFDA), Zanzibar, Tanzania.*
[4]*Medicine Policy Unit, Ministry of Health, Zanzibar, Tanzania.*
[5]*Department of Pharmacology, State University of Zanzibar, Tanzania.*

Article Info:

Article History:
Received: 22 December 2025
Reviewed: 9 January 2026
Accepted: 17 February 2026
Published: 15 March 2026

Cite this article:
Said SS, Zulfa N, Bhimajiyan G, Okafor CJ, Simai B, Rashid SS, Ibrahim AS, Mwaddini AM, Majethia H, Desu PK. Formulation and evaluation of fast dissolving herbal film containing reserpine for the management of pulmonary arterial hypertension. Universal Journal of Pharmaceutical Research 2026; 11(1): 7-13. ***http://doi.org/10.22270/ujpr.v11i1.1483***

***Address for Correspondence:**
Said Salim, Zanzibar Food and Drug Agency, Zanzibar, Tanzania. Tel: +255777594373
E-mail: *saidalriyamy67@gmail.com*

Abstract

Background and Objectives: Pulmonary arterial hypertension is a progressive disease of the pulmonary vasculature that is defined by a high pulmonary vascular resistance, which ultimately causes a failure of the right heart. Reserpine is a biologically active compound that is derived from *Rauwolfia serpentina*. It is known for its potent antihypertensive activity. Therefore, reserpine can be considered a new way of treating pulmonary arterial hypertension. The objectives of the study were to formulate and evaluate the Fast Dissolving Films (FDF) of reserpine using the newly developed polymeric delivery system.
Methods: Reserpine FDFs were prepared using hydroxypropyl methyl cellulose K-15 as the polymeric film former and propylene glycol as the plasticizer using the solvent casting method. Various physicochemical parameters like pH, weight variation, folding endurance, disintegration time, content uniformity, and *in vitro* dissolution were carried out. Compatibility analysis was carried out using FT-IR. Compatibility between the drug and the polymer was analyzed using Differential Scanning Calorimetry.
Results: These films were transparent, flexible, strong, evenly 0.12-0.17mm thick, with surface pH range compatible with that of the oral cavity (6.0-6.7). The values of folding endurance were above 50 cycles, which shows very strong tensile strength. The disintegration time ranges from 15-66 sec, with the optimized formula (F6) having 97.5% release of the drug in 40 minutes. The DSC scans showed molecular distribution of reserpine with slight reduction of the drug's peak at 63.90°C, thus ensuring the drug is dissolved without degrading to ensure increased bioavailability.
Conclusion: The FTIR spectrogram proves that reserpine is chemically stable in the polymer matrix. Prepared films possess the optimal physico-chemical properties, disintegration times, and dissolution profiles. Hence, the formulation approach demonstrates immense promise for the systemic delivery of the herbal antihypertensive in the treatment of PAH.
Keywords: Fast-dissolving films, herbal formulation, pulmonary arterial hypertension, *Rauwolfia serpentina*, reserpine.

INTRODUCTION

Pulmonary Arterial Hypertension (PAH) is a progressive, debilitating disease that can lead to fatal outcome, characterized by increased pressure in the pulmonary artery, which in the long run leads to right-sided heart failure, causing premature death[1,2]. PAH is usually observed in women of childbearing age and is classified as a rare disease, with an approximated prevalence of 15-50 per million populations. The hemodynamic definition of PAH can only be measured using the right heart catheterization procedure, which is characterized by increased Mean Pulmonary Artery Pressure (mPAP ≥25 mmHg at rest), Pulmonary Artery Wedge Pressure≤15 mmHg, and increased Pulmonary

Vascular Resistance (PVR≥3 Wood units[3]. PAH is a disease of low prevalence but high burden[4].

Prior to the availability of therapies targeted to PAH, the disease's prognosis was dismal, with a survival rate estimated at about 69% at one year and 38% survival at five years[5]. Although the development of therapies targeting the underlying pathophysiological processes in PAH has greatly improved survival and symptoms, it should be kept in mind that PAH is, nonetheless, a progressive and fatal disease, in which disease progression is all too common[6]. Perhaps the most characteristic histopathological feature of PAH is the severe remodeling of the distal pulmonary arterioles, which includes either medial hypertrophy, intimal fibrosis, smooth muscle cell proliferation, or myofibroblast accumulation[7]. Moreover, a hallmark of severe disease is the development of plexiform lesions, which are ectatic vascular channels formed due to disordered growth of the pulmonary vascular endothelial cells, thereby causing obstruction in pulmonary blood flow[8]. Other abnormalities, such as excess collagen, fragmentation of the elastic lamina, or disorganization of the extracellular matrix, also contribute significantly to vascular narrowing[9].

Endothelial dysfunction due to genetic predisposition and exposure to environment factors has been thought to be the first step towards pathogenesis in patients with PAH. Injury of pulmonary microvessel endothelium results in an imbalance between vasoconstrictors and vasodilators, contributing towards an inflammatory process, thrombosis, and vascular repair. Contemporary treatments for PAH, which involve vasodilators, are focused on an intact pulmonary vascular bed to improve hemodynamic parameters[10,11]. Contemporary treatments for PAH have improved survival indices for up to 85% at one year and 57% at five years. However, there has not been an effective reversal of vascular remodeling or restoration of microvessels, which has led to progression towards pulmonary failure in these patients and hence pulmonary transplantation being the only alternative for survival[12]. It becomes an utmost need for more effective therapeutic modalities that can help in better improvement of survival indices[13].

Indeed, observational studies from major registries provide more insight into the dynamically shifting context of PAH management. Initial observations from the National Institutes of Health (NIH) registry (1981-1985) suggested a survival of only 2.8 years, with a five-year survival of only 34%[14]. However, more contemporary registries like the French PAH Registry, REVEAL Study from the United States, document improved survival rates, underscoring the advances made in the diagnosis, treatment, and subsequent care of patients with this disease. Indeed, the REVEAL Study reported survival rates of about 91% after the first year, 85% after the third, and 68% after five years of survival[15]. Though this indicates better survival rates, unfortunately, this remains less than optimal, with disease progression remaining a daunting clinical task[16].

PAH is, in a general way, a condition that causes nonspecific symptoms, which in most cases delays diagnosis until late in the condition. These symptoms include exertional dyspnea, Symptoms may also include signs related to right heart failure in the advanced stages, which may include abdominal distention, jugular venous distention, peripheral edema, chest pain, and syncope[17]. The World Health Organization functional classification is the general classification used in the estimation of the degree of the condition, which varies from one person to another depending on the severity. Transthoracic echo-cardiography is mainly useful as the testing agent in the screening process[18].

In the therapeutic management of PAH, there are three major signaling pathways that have been identified as targets, and these include the NO pathway, the endothelin pathway, and the prostacyclin pathway. For therapeutic purposes, the pharmacological targets that have been developed include phosphodiesterase-5 inhibitors, stimulators of soluble guanylate cyclase, endothelin receptor antagonists, prostacyclins and their analogues, and finally, prostacyclin receptor agonists[19]. Despite the fact that the pharmacological agents have been improved upon by the inclusion of combination therapies in reducing the morbidity and mortality rates, the fact still remains that the patients continue to progress despite the available therapies[19,20].

In such a realm, there is great interest in finding complementary/alternative treatments like herbal drugs, which have proven cardioactive properties. *R. serpentina* is a known traditional medication used in the treatment of hypertension and cardiovascular disease[21,22]. Its most active alkaloid, reserpine, is used in the management of hypertension because it selectively inhibits the vesicular monoamine transporter-2 (VMAT-2); this causes a depletion in the central and peripheral sympathetic terminal catechol-amines, resulting in a consequent decrease in peripheral resistance, heart rate, and cardiac output. However, this compound’s usefulness is hampered by slow onset, high first-pass effect, and accompanying toxic effects[23].

Fast-dissolving films (FDFs) have been developed as an innovative oral drug delivery technology that can disintegrate easily in the oral cavity without the use of water[24]. There are many advantages to using these films, including increased compliance, rapid onset of action, higher bioavailability, and avoidance of the first-pass effect through possible buccal absorption[25]. The oral cavity has highly permeable and highly vascular tissue, thereby offering great advantages in the systemic administration of drugs[26]. Fast-dissolving films were initially designed for patients having difficulty in swallowing, particularly in pediatrics and geriatrics[27].

Keeping the aforementioned aspects in mind, the current research work will attempt to formulate and characterize an innovative fast dissolving herbal film containing reserpine as its active ingredient to treat pulmonary arterial hypertension. This will be the first attempt to utilize an established herb used in the treatment of hypertension in conjunction with the most advanced form of fast dissolving technology.

MATERIALS AND METHODS

The film-forming polymer employed for this study was hydroxypropyl methylcellulose (HPMC K15). It was plasticized with propylene glycol. Other additives employed for this study were citric acid, menthol, and fructose. Analytical grades of these chemical compounds were employed[28,29].

Pre-formulation studies were carried out to evaluate the physicochemical characteristics of reserpine and to obtain the necessary information for the formulation. Reserpine was tested for color, odor, and appearance under normal light. The identification of reserpine is carried out to confirm whether the reserpine used contains impurities and irregularities in the appearance of the drug.

Compatibility studies

Compatibility studies were carried out to evaluate the chemical stability of the reserpine drug in the presence of the formulation excipients[30].

Fourier Transform Infrared (FTIR)

The FTIR test was carried out to evaluate the functional groups present in the drug using the FTIR instrument. The excipients used in the formulation were also analyzed using the FTIR instrument to evaluate the functional groups present in the excipients. The FTIR instrument was used to evaluate the functi-onal groups present in the drug. The excipients used in the formulation were also analyzed spectro-scopy was used to identify the characteristic groups of the drug, as well as the potential interaction that might exist between the drug and the excipients. FTIR spectra of the drug, the mixture of the drug with excipients, and the ideal mixture were obtained[31].

Differential Scanning Calorimetry

The differential scanning calorimetry technique was used to study the thermal properties of the drug, especially the miscibility of the drug with HPMC K15. Weighed amounts of the powdered drug and physical mixtures of the drug with HPMC K15 were placed in aluminum pans, with another pan used as the reference. The pans were scanned from 30°C to 265°C using a 5°C/min heat rate with nitrogen current. The thermograms were used to observe the peak shift, which is indicative of drug-polymer interaction or the development of the melting points of the drug[32].

Preparation of fast-dissolving herbal films

Fast-dissolving films containing the drug reserpine were prepared using the solvent casting method (Table 1). A precise amount of HPMC K15 was mixed with double-distilled water using magnetic stirring to form a viscous solution of the polymer. Plasticizer propylene glycol was added to the mixture, followed by menthol, citric acid, fructose, and reserpine, which were added to the mixture with constant stirring[33].

The prepared solution was then allowed to stand for removing entrapped air bubbles and then poured onto a clean glass plate to prepare a cast. The cast was then dried at ambient conditions for a period of 24 hours. The resulting films were then carefully removed, cut into equal squares of size 2x2 cm², and then stored in desiccators for further testing[34].

Experimental design

The experimental design used to carry out the optimization of the fast-dissolving films was the 3^2 full factorial designs. In the experimental design, the independent variables that were examined using three different levels (low, medium, and high) included the amount of HPMC K15 (X_1) and the amount of propylene glycol (X_2). The dependent variable chosen for the experiment was the release of the drug. There were nine experimental formulations (F1 to F9)[35].

Evaluation of fast dissolving films

The analysis of the color, transparency, flexibility, and surface smoothness of the films was carried out[37].

Film thickness

The thickness of the film was determined by measuring the thickness of the film at three distinct points using a Vernier caliper. The average thickness of the film was calculated[37].

Weight

Each film was individually analyzed by determining the mean weight of the three film samples using an analytical balance[37].

Surface

The pH value of the surface of the film was determined by placing the film on a wet glass slide. The pH value was assessed using a digital pH meter for the compatibility of the mucosa[37].

Folding endurance

A 2 x 2 cm² film was folded at the same spot until the film tore. The number of folds until the film tore is known as the folding endurance of the film[37].

***In-vitro* disintegration**

The film was kept in a Petri dish containing a phosphate buffer solution of pH 6.8. The petri dish was kept in a water bath at a temperature of 37°C±0.5°C. The time taken for the film to disintegrate completely was noted[38].

***In vitro* dissolution**

The film was kept in a basket containing a phosphate buffer solution of 300 mL capacity with a pH of 6.8 and a temperature of 37±0.5°C. The basket was kept in a USP basket apparatus rotating at a speed of 50rpm. The samples of 5 mL were withdrawn at intervals of 5, 10, 20, 30, and 40 minutes and examined using a UV-Vis spectrophotometer at a wavelength of 216 nm[39].

Drug content uniform

The film was dissolved in a phosphate buffer solution of pH 6.8. The concentration of the drug was determined using a UV-Vis spectrophotometer at a wavelength of 216 nm with a calibration curve of 2 to 10 µg/mL[37].

RESULTS

The FTIR spectrum of pure reserpine showed distinct peaks at 3268 cm^{-1} (N-H), 2924 cm^{-1} (C-H), and 1668 cm^{-1}(C=N), confirming its chemical structure (Figure 1). These peaks matched the standard reference value, verifying the purity and integrity of reserpine; no unexpected bands were detected, indicating the compound was chemically stable. When reserpine was combined with HPMC K15, all characteristic peaks remained with only minor shifts. This suggested

secondary interaction, like hydrogen bonding, no chemical reaction occurred. So the formulations thus exhibited excellent drug-polymer compatibility. The FTIR spectrum of the optimized FDF retained all prominent reserpine peaks. No disappearance or formation of new peaks was observed, confirming stability during formulation. This proved that the reserpine chemical structure was preserved in the final film.

In the DSC result, there was a strong endothermic point at a temperature of 63.90°C (Figure 2). This was close to the melting point of reserpine of 65°C. The presence of a strong endothermic transition point at a temperature of 231.93°C in the DSC result of the HPMC K15 indicated a strong melting point of the polymer. The result indicated a high degree of thermal stability of the polymer. There were no additional points in both of the thermograms. The optimized FDF showed some variations and reduction in the intensity of the melting point peak of reserpine. This confirmed the partial amorphization of the drug reserpine, which is soluble by dissolution. There were no additional peaks detected. This confirms the absence of incompatibility or decomposition.

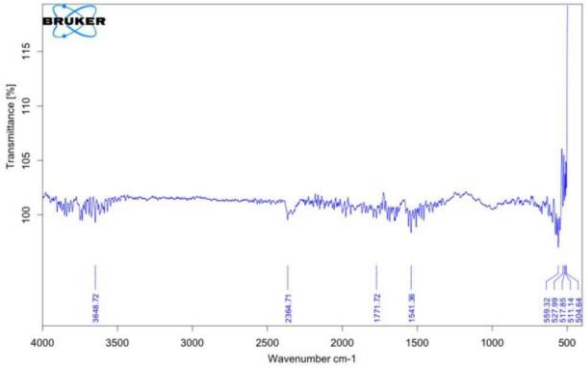

Figure 1: Infrared spectrum of Reserpine, and HPMC K15.

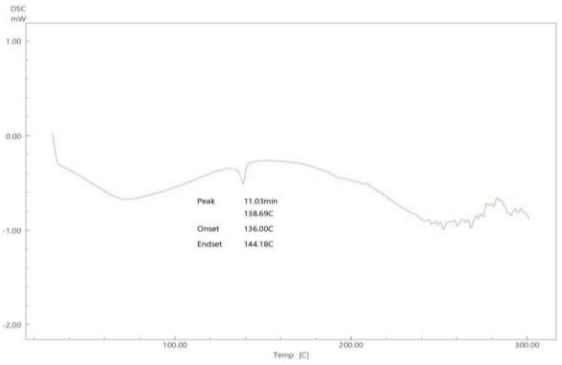

Figure 2: Differential Scanning Calorimetry (DSC) of reserpine and HPMC K15.

All film samples were homogeneous and flexible, with no breaks or voids in their formulations. These features revealed a homogenous distribution of reserpine in polymeric matrices. The film thickness ranged from 0.122 mm to 0.17 mm, while the average weighted amount ranged from 26 mg to 132 mg (Table 2). The slight variation in measurements demonstrated that the solvent casting process produced consistent results. The pH of these surfaces (6.0-6.7) was close to neutral, reducing the risk of irritation during administration. All the films showed folding endurance above 50 indicating adequate flexibility and mechanical stability for packaging/handling.

The *in-vitro* disintegration times ranged from 154 to 66 seconds, which met the requirement for a fast-release form an optimized batch (F6) that exhibited a disintegration time of about 40 sec. Dissolution studies showed faster dissolution from all formulations, with more than 80% of COM released within 40 minutes (Table 3).

Table 1: Formulation of herbal fast formulation films containing reserpine.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Reserpine (mg)	7	7	7	7	7	7	7	7	7
HPMC K15 (mg)	400	400	400	500	500	500	600	600	600
Propylene glycol (ml)	1.5	1	2	1.5	1	2	1.5	1	2
Citric Acid (mg)	6	6	6	6	6	6	6	6	6
Menthol (mg)	10	10	10	10	10	10	10	10	10
Fructose (mg)	6	6	6	6	6	6	6	6	6
Distilled water	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs

Table 2: Evaluation parameters of reserpine containing FDFs.

Formulation	pH	Thickness (mm)	Average weight variation (mg)	Folding Endurance	Disintegration Time (sec)
F1	6.65	0.15	26.333	35	15
F2	6.66	0.12	47.667	42	32
F3	6.61	0.14	32.667	50	25
F4	6.6	0.13	67.667	56	35
F5	6.65	0.15	67.233	63	54
F6	6.63	0.17	88.00	55	40
F7	6.7	0.15	55.333	64	66
F8	6.3	0.17	62.333	45	40
F9	6	0.16	131.667	66	44

Table 3: Cumulative % drug release of FDFs.

Time(min)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	3	19.16	44.72	6.94	4.72	14.49	9.72	1.94	3.61
10	5.3	42.77	64.16	16.94	45	72.22	32.5	11.94	38.61
20	37.2	65.27	72.5	36.38	36.66	74.73	38.61	15.83	61.38
30	62.5	65.88	92.5	46.94	65.83	80.27	61.94	57.5	64.44
40	78.33	66.38	93.3	66.94	91.94	97.5	74.44	60.83	77.77

The optimized formulation F6 showed 97.5% drug release after 40 minutes, due to good solubilization and dispersion of reserpine. Drug content uniformity was determined by dissolving precisely weighed film in phosphate buffer (pH 6.8), followed by absorbance measurement at 216nm relative to a standard calibration curve of reserpine (2-10 µg/ml; R^2=0.9).

DISCUSSION

In this respect, the reserpine- loaded fast-dissolving herbal films prepared in this study possessed improved physicochemical, mechanical, and biopharmaceutical properties, thereby proving the formulation efficacy of the solvent casting technique for preparing the oral fast-dissolving films containing *R. serpentina* active constituent[37,38]. Scanning electron microscopic analysis indicated that the films had a smooth, homogeneous surface with a uniform distribution of reserpine, the lack of cracks, empty spaces, and minimal differences in weight between the batches, thereby indicating the precise control over the viscosity of the polymer solution in this study[37].

In-vitro disintegration test analyses revealed rapid hydration and polymer relaxation; the disintegration times varied between 66 and 154 seconds; interestingly, the optimized formulation (F6) disintegrated in around 40 seconds[38]. Such rapid disintegration is due to the hydrophilic character of HPMC K15 and the optimized ratio between the polymer and plasticizer. This enables rapid aqueous entry and subsequently rapid drug release.

Additionally, the dissolution studies supported the efficacy and effectiveness of the matrix. Interestingly, the optimized film Pros-F40 released 97.5% cumulative reserpine in 40 minutes[38]. These properties and phenomena find significant application in the treatment of PAH, where rapid pharmacological response is quite essential[39].

The physicochemical stability and compatibility of the films were confirmed by FTIR and thermal analysis. The result of FTIR revealed that there was a minor shift in the characteristic peaks of the respective groups, which expressed hydrogen bonding or non-covalent bonding between the two materials, thereby facilitating dispersion at the molecular level of the herbal drug reserpine into polymeric films without affecting the stability of the drugs[40]. The result of the DSC analysis confirmed that there was no change in the physicochemical stability of HPMC K15 polymer, with a minor decrease in the intensity with a peak at 63.90°C of the endothermal peak of the drug, thereby expressions of enhancement in solubility and bioavailability of drugs[41].

Molecular level dispersion of drugs is a new approach, where a traditional herbal component has been integrated with a cutting-edge delivery system to enhance therapeutic properties[41]. The above evidences thereby confirmed that there was a potential of chemically stabilized, mechanically strong, and biopharmaceutically optimal prepared fast dispersible herbal films, which could play a significant role as a patient-friendly, non-invasive drug delivery system to enhance the existing condition of pulmonary arterial hypertension with proper utilization of a traditional important herbal component.

CONCLUSIONS

The current study was successful in formulating and characterizing the fast-dissolving herbal films containing the active compound reserpine (*R. serpentina*), signifying the strong B-plasticizing property of propylene glycol to the HPMC K15 polymer chains. Fast disintegration and high *in vitro* dissolution efficiency were obtained through the molecular level dispersion of reserpine. This study formulates something new – a mechanically optimized approach towards a non-invasive and clinically significant therapeutic approach. These findings emphasize its ability to improve patient compliance, speed of therapeutic intervention, and cardiovascular efficacy, making it an essential tool in the present state of medicinal research and developments.

ACKNOWLEDGEMENTS

The authors sincerely thank the Marwadi University Faculty of Pharmacy for providing the laboratory facilities and technical assistance throughout this study. Special gratitude is extended to the colleagues and staff for their support during the formulation and analytical procedures. The authors acknowledge the supplies of reserpine for providing quality materials. Finally, appreciation goes to all who contributed directly or indirectly to the successful completion of this research.

AUTHOR'S CONTRIBUTIONS

Said SS: writing original draft, formal analysis, conceptualization. **Zulfa N:** writing original draft, data organization. **Bhimajiyan G:** conceptualization, supervision, data organization. **Okafor CJ:** conceptualization, data organization. **Simai B:** critical review. **Rashid SS:** validation. **Ibrahim AS:** data curation. **Mwaddini AM:** validation. **Majethia H:** data curation, validation. **Desu PK:** data organization,

validation. Final manuscript was checked and approved by all authors.

DATA AVAILABILITY

The datasets generated or analyzed during this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The author declares there are no conflicts of interest.

REFERENCES

1. Oudiz RJ. Death in pulmonary arterial hypertension. Am J Respir Crit Care Med 2013; 188(3): 269-270. *https://doi.org/10.1164/rccm.201305-0898ED*
2. Tonelli AR, Arelli V, Minai OA, *et al*. Causes and circumstances of death in pulmonary arterial hypertension. Am J Respir Crit Care Med 2013; 188(3): 365-369. *https://doi.org/10.1164/rccm.201209-1640OC*
3. Dubroff J, Melendres L, Lin Y, *et al*., High geographic prevalence of pulmonary artery hypertension: Associations with ethnicity, drug use, and altitude. Pulm Circ 2020; 10:1. *https://doi.org/10.1177/2045894019894534*
4. Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: Identification of the most accurate estimates from a systematic literature review. Pulm Circ 2021; 11(1):20458940-20977300. *https://doi.org/10.1177/2045894020977300*
5. O'Callaghan DS, Humbert M. A critical analysis of survival in pulmonary arterial hypertension. Eur Respir Rev 2012; 21(125): 218-222.*https://doi.org/10.1183/09059180.00003512*
6. Emmons-Bell S, Johnson C, Boon-Dooley A, *et al*. Prevalence, incidence, and survival of pulmonary arterial hypertension: A systematic review for the global burden of disease 2020 study. Pulm Circ 2022; 12(1): e12020. *https://doi.org/10.1002/pul2.12020*
7. Pietra GG, Edwards WD, Kay JM, *et al*. Histopathology of primary pulmonary hypertension. A qualitative and quantitative study of pulmonary blood vessels from 58 patients in the National Heart, Lung, and Blood Institute, Primary Pulmonary Hypertension Registry. Circulation 1989; 80(5): 1198-1206. *https://doi.org/10.1161/01.CIR.80.5.1198*
8. Lee JY, Francis CM, Bauer NN, *et al*. A cancer amidst us: The plexiform lesion in pulmonary arterial hypertension. Am J Physiol - Lung Cell Mol Physiol 2020; 318(6): L1142-L1144. *https://doi.org/10.1152/ajplung.00092.2020*
9. Jia Z, Wang S, Yan H, *et al*. Pulmonary vascular remodeling in pulmonary hypertension. J Pers Med 2023; 13(2): 366. *https://doi.org/10.3390/jpm13020366*
10. Kurakula K, Smolders VFED, Tura-Ceide O, *et al*. Endothelial dysfunction in pulmonary hypertension: Cause or consequence ? Biomed 2021; 9(1): 57. *https://doi.org/10.3390/biomedicines9010057*
11. Marinho Y, Villarreal ES, Loya O, *et al*. Mechanisms of lung endothelial cell injury and survival in pulmonary arterial hypertension. Am J Physiol - Lung Cell Mol Physiol 2024; 327(6): L972-L983. *https://doi.org/10.1152/ajplung.00208.2024*
12. O'Callaghan DS, Humbert M. A critical analysis of survival in pulmonary arterial hypertension. Eur Respir Rev 2012; 21(125): 218-222. *https://doi.org/10.1183/09059180.00003512*
13. Flores CV, Chan SY. Therapeutic targets for pulmonary arterial hypertension: Insights into the emerging landscape. Expert Opin Ther Targets 2025; 29(6): 327-343. *https://doi.org/10.1080/14728222.2025.2507034*
14. Farber HW, Miller DP, Poms AD, *et al*. Five-year outcomes of patients enrolled in the reveal registry. Chest 2015; 148(4): 1043-1054. *https://doi.org/10.1378/chest.15-0300*
15. Pauwaa S, Machado RF, Desai AA. Survival in pulmonary arterial hypertension: A brief review of registry data. Pulm Circ 2011; 1 (3): 430-431; 2011. *https://doi.org/10.4103/2045-8932.87314*
16. Suranjan B, Deekshit A, Bala YKS, Teja GB. A case study on reduction of lung functions in patients with diabetes mellitus in Andhra Pradesh, India. Universal J Pharm Res 2021; 6(5):74-76. *https://doi.org/10.22270/ujpr.v6i5.676*
17. Singh S, Virmani T, Virmani R, Kumar P, Mahlawat G. Fast dissolving drug delivery systems: Formulation, preparation techniques and evaluation. Universal J Pharm Res 2018; 3(4): 56-64. *https://doi.org/10.22270/ujpr.v3i4.185*
18. Chauhan V, Kumar K, Teotia D. Fast dissolving tablets: A promising approach for drug delivery. Universal J Pharm Res 2017; 2(4): 51-57. *http://doi.org/10.22270/ujpr.v2i4.RW4*
19. Thenappan T, Shah SJ, Rich S, *et al*. Survival in pulmonary arterial hypertension: A reappraisal of the NIH risk stratification equation. Eur Respir J 2010; 35(5): 1079-1087. *https://doi.org/10.1183/09031936.00072709*
20. Pauwaa S, Machado RF, Desai AA. Survival in pulmonary arterial hypertension: A brief review of registry data. Pulm Circ 2011; 1(3): 430-431. *https://doi.org/10.4103/2045-8932.87314*
21. Xue Z, Li Y, Zhou M, Liu Z, *et al*. Traditional herbal medicine discovery for the treatment and prevention of pulmonary arterial hypertension. Front Pharmacol 2021; 12:720873. *https://doi.org/10.3389/fphar.2021.720873*
22. Xiang L, Li Y, Deng X, *et al*. Natural plant products in treatment of pulmonary arterial hypertension. Pulm Circ 2018; 8:3. 2018. *https://doi.org/10.1177/2045894018784033*
23. Akhtar MS. Formulation and evaluation of fast dissolving tablets of antiepileptic drug. Universal J Pharm Res 2019; 4(6):20-24. *https://doi.org/10.22270/ujpr.v4i6.331*
24. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. Int J Pharm Investig 2013; 3(2): 67-76. *https://doi.org/10.4103/2230-973X.114897*
25. Chidi E, Nwobodo NN, Offiah RO. Development and evaluation of fast dissolving thin films of aripiprazole. Universal J Pharm Res 2017; 2(5): 19-23. *http://doi.org/10.22270/ujpr.v2i5.R5*
26. Ahmed EM, Ibrahim ME, Magbool FF. *In vitro-in vivo* bio-equivalence correlation study of atenolol, and its brands of immediate release tablet under bio-waiver conditions. Universal J Pharm Res 2019; 4(6):25-29. *https://doi.org/10.22270/ujpr.v4i6.332*
27. Ahmed EM, Ibrahim ME, Magbool FF. *In vitro-in vivo* bio-equivalence correlation study of metronidazole, and its brands of immediate release tablet under bio-waiver conditions. Universal J Pharm Res 2020; 5(1): 32-37. *https://doi.org/10.22270/ujpr.v5i1.360*
28. Opeyemi OT, Adegbenro OO. Development and characterization of direct compressed matrix mini tablets of naproxen sodium. Universal J Pharm Res 2018; 3(5): 63-68. *https://doi.org/10.22270/ujpr.v3i5.205*
29. Ali A, Alsaifi A. Quality control assessment of different brands of ciprofloxacin 500 mg tablets in Yemen. Universal J Pharm Res 2018; 3(4): 29-33. *https://doi.org/10.22270/ujpr.v3i4.175*
30. Prajapati S, Patel L, Patel C. Floating matrix tablets of domperidone formulation and optimization using simplex lattice design. Iran J Pharm Res 2011; 10(3): 447-455, 2011.
31. Verma BK, Pandey S, Arya P. Tablet granulation: current scenario and recent advances. Universal J Pharm Res 2017; 2(5): 30-35. *http://doi.org/10.22270/ujpr.v2i5.RW1*
32. Rajagopalan S, Rajendhiran D, Mohamed IA, Sherbudeen SB. Fast dissolving oral thin films: An innovative herbal drug delivery system. Int J Res Med Sci 2024; 12(8):3085-3090. *https://doi.org/10.18203/2320-6012.ijrms2024225*
33. Touqeer SI, Jahan N, Abbas N, Ali A. Formulation and process optimization of rauvolfia serpentina nanosuspension by HPMC and *in vitro* evaluation of ACE inhibitory potential. J Funct Biomater 2022; 13(4): 268. *https://doi.org/10.3390/jfb13040268*
34. Andrew EC, Grace EA, Izuchukwu BC, Chinemerem OE, Onunkwo G. Evaluation of oro-dispersible tablets (Artemether-Lumefantrine and Amoxicillin trihydrate) used for some common childhood diseases (malaria and pheumonia). Universal J Pharm Res 2022; 7(4):32-37. *https://doi.org/10.22270/ujpr.v7i4.812*

35. Alzomor AKY, Al-Madhagi WM, Aljbry M, Almontser S, Al-Absi S, Khalid M. *In-vitro* bioequivalence study for marketed innovator and three brands local manufacturing ciprofloxacin hydrochloride tablets in Yemen. Universal J Pharm Res 2022; 7(5):12-17. *https://doi.org/10.22270/ujpr.v7i5.835*
36. Maad AH, Shayoub MEA, Elnima EI, Osman Z, Magbool FF. Formulation and evaluation of colon targeted matrix tablets containing extract of *Solenostemma argel* (Hargel). Universal J Pharm Res 2019; 4(4): 33-38. *https://doi.org/10.22270/ujpr.v4i4.297*
37. Vlad RA, Pintea A, Pintea C, *et al*. Hydroxypropyl methylcellulose-A key excipient in pharmaceutical drug delivery systems. Pharmaceutics 2025; 17(6): 784. *https://doi.org/10.3390/pharmaceutics17060784*
38. Nweje-Anyalowu PC, Anyalogbu EAA, Jim WA.Design and evaluation of chronotherapeutic pulsatile drug delivery system of Cilnidipine. Universal J Pharm Res 2017; 2(5): 15-18. *http://doi.org/10.22270/ujpr.v2i5.R4*
39. Aguila MAL, Xu Y, Wang Y, *et al*. Balanced biocompatibility in high-viscosity hydroxypropyl methylcellulose-based sponge containing nanoconfined silver citrate nanoparticles. Int J Biol Macromol 2025; 327:147534. *https://doi.org/10.1016/j.ijbiomac.2025.147534*
40. Rana R, Madaan R, Bala R. Formulation design and optimization of sustained released matrix tablets of Propranolol HCl using natural and synthetic polymers. Acta Pharm Sci 2021; 59(2): 321-341. *https://doi.org/10.23893/1307-2080.APS.05920*
41. Dewi MK, Chaerunisaa AY, Muhaimin M, Joni IM. Improved Activity of herbal medicines through nanotechnology. Nanomaterials 2022; 12(22): 4073. *https://doi.org/10.3390/nano12224073*