

## Revitalizing COPD Management: Exploring Drug Repurposing as a Promising Therapeutic Paradigm

Deepakumari V\*, G Selvi

Department of Pharmaceutics, C L Baid Metha college of Pharmacy, Thoraipakkam, The Tamil Nadu, Dr. M.G.R. Medical University, Chennai 600097 Tamil Nadu, India

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### Abstract



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Chronic Obstructive Pulmonary Disease (COPD) is a prevalent and debilitating respiratory condition, necessitating ongoing exploration for innovative therapeutic strategies. This comprehensive review delves into the realm of drug repurposing as a promising avenue to expand therapeutic options for managing COPD. The pursuit of novel COPD treatments has prompted researchers to reassess existing drugs approved for other indications, leveraging their established safety profiles and mechanisms of action. Within this review, we examine a spectrum of repurposed drugs, including anti-inflammatory agents, bronchodilators, antioxidants, and more, shedding light on their potential benefits in COPD management. Additionally, we discuss clinical trials and real-world evidence supporting the efficacy and safety of repurposed drugs in COPD, emphasizing the urgency of finding cost-effective solutions to alleviate the socioeconomic burden of COPD. This review provides a comprehensive overview of the current state of drug repurposing in COPD therapy, highlighting its potential to enhance patient care and alleviate the global burden of this chronic respiratory ailment.

### \*Corresponding Author

Name: Deepakumari V  
Phone: +91 8220941818  
Email: deepavenkat2210@gmail.com

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### INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive lung disorder characterized by persistent airflow limitation and respiratory symptoms, such as cough, wheezing, and

shortness of breath. It is a leading cause of morbidity and mortality worldwide, posing a significant burden on global health. COPD is primarily caused by long-term exposure to harmful particles or gases, most commonly from cigarette smoke. The disease is associated with substantial economic costs, reduced quality of life, and increased healthcare utilization. According to the World Health Organization, COPD is projected to become the third leading cause of death globally by 2030. Effective management and the exploration of new therapeutic options are crucial to alleviate the impact of COPD on individuals and societies [1].

Expanding therapeutic options in COPD management is imperative due to several reasons. Firstly, the existing treatments for COPD, such as

bronchodilators and corticosteroids, primarily focus on symptom relief and slowing disease progression but do not offer a cure. Secondly, not all patients respond adequately to current therapies, highlighting the need for personalized treatment approaches. Additionally, COPD is a complex disease with various underlying mechanisms, including inflammation, oxidative stress, and immune dysregulation. Expanding therapeutic options can target these diverse pathways and potentially provide more effective and tailored interventions. Furthermore, the availability of new treatments can enhance patient outcomes, improve quality of life, reduce exacerbations, and alleviate the socioeconomic burden associated with COPD [2].

Drug repurposing, also known as drug repositioning or drug rediscovery, refers to the exploration of existing drugs approved for one medical condition to be repurposed for the treatment of another condition. This approach offers several advantages in COPD treatment. Firstly, repurposing eliminates the lengthy and costly drug development process, making it a faster and more cost-effective strategy. Secondly, repurposed drugs have already undergone safety and toxicity assessments, reducing potential risks and allowing for quicker clinical translation. Additionally, repurposed drugs may target novel pathways or mechanisms involved in COPD pathogenesis, providing alternative therapeutic options beyond traditional treatments. Overall, drug repurposing holds the potential to expedite the availability of new therapeutic options for COPD patients [3].

### **Pathophysiological Processes in COPD**

COPD is characterized by a complex interplay of pathophysiological processes that contribute to disease development and progression. Chronic exposure to harmful particles or gases, primarily from cigarette smoke, leads to persistent inflammation in the airways and lung tissue. This inflammatory response involves the recruitment of immune cells, release of inflammatory mediators, and activation of proteases, resulting in tissue damage and remodeling. Oxidative stress, induced by an imbalance between reactive oxygen species and antioxidant defenses, further exacerbates lung injury. Over time, these processes lead to airway narrowing, mucus

hypersecretion, destruction of alveolar walls, and loss of lung elasticity, leading to airflow limitation and respiratory symptoms in COPD patients [4].

### **Immune Dysregulation in COPD Development and Progression**

Inflammation, oxidative stress, and immune dysregulation play critical roles in the development and progression of COPD. Chronic exposure to harmful particles or gases triggers an inflammatory response in the lungs, characterized by the recruitment and activation of immune cells, including neutrophils, macrophages, and T lymphocytes. This persistent inflammation leads to tissue damage, airway remodeling, and mucus hypersecretion. Oxidative stress, resulting from an imbalance between reactive oxygen species and antioxidant defenses, further amplifies the inflammatory response and promotes lung injury. Immune dysregulation, including impaired immune cell function and aberrant cytokine production, contributes to chronic inflammation and tissue destruction in COPD. Targeting these pathways holds promise for developing effective therapies for COPD management [5].

### **Brief Overview of Current Pharmacological Interventions**

Current pharmacological interventions for COPD primarily include bronchodilators, such as beta-agonists and anticholinergics, which relax the airway smooth muscles and improve airflow. Inhaled corticosteroids may be prescribed in combination with bronchodilators to reduce airway inflammation. Additionally, medications targeting specific inflammatory pathways, such as phosphodiesterase-4 inhibitors, can be used to reduce exacerbations. Non-pharmacological interventions for COPD management involve lifestyle modifications and supportive therapies. Pulmonary rehabilitation programs focus on exercise training, education, and self-management strategies to improve exercise capacity and quality of life. Oxygen therapy, vaccination against respiratory infections, and smoking cessation interventions are also vital components of COPD care. Surgical interventions, such as lung volume reduction surgery or lung transplantation, may be considered in severe cases [6].

### **Limitations and Challenges Associated with Existing Therapies**

Existing therapies for COPD face several limitations and challenges. Firstly, while bronchodilators provide symptomatic relief and improve airflow, they do not alter the underlying disease progression. Inhaled corticosteroids, commonly used for reducing inflammation, may have limited efficacy in certain COPD subtypes. Moreover, long-term use of corticosteroids can be associated with systemic side effects. Medication adherence can be challenging due to complex inhaler techniques and regimen complexity. Additionally, some patients may exhibit poor response or resistance to available treatments. The high cost of certain medications can also limit accessibility, especially in low-resource settings. Novel therapies are needed to address these limitations and provide more effective and personalized treatment options for COPD patients [7].

### **Explanation of the Concept of Drug Repurposing and its Advantages**

Drug repurposing, also known as drug repositioning, refers to the practice of identifying new therapeutic uses for existing drugs that were originally developed and approved for different indications. Instead of starting from scratch, drug repurposing capitalizes on the existing knowledge of safety profiles, pharmacokinetics, and potential mechanisms of action of approved drugs. This approach offers several advantages, including reduced development time and costs, as extensive preclinical and early clinical testing has already been conducted. Repurposed drugs also have the potential for accelerated regulatory approval and a shorter path to clinical implementation, providing expedited access to new treatment options for patients [8].

### **Rationale for Exploring Repurposed Drugs in COPD Treatment**

Exploring repurposed drugs in COPD treatment offers a compelling rationale for several reasons. Firstly, COPD is a complex disease with multiple underlying mechanisms, including inflammation, oxidative stress, and immune dysregulation. Repurposed drugs, which have already been approved for other indications, may target these specific pathways, providing a potential therapeutic benefit in COPD. Secondly, repurposing existing drugs saves time and resources by bypassing the lengthy drug

development process, accelerating their availability for COPD patients. Additionally, repurposed drugs have established safety profiles, reducing the risks associated with novel drug development. Overall, repurposing offers a promising strategy to expand the therapeutic options in COPD management [9].

### **Various Approaches and Methodologies used in Drug Repurposing Studies**

Drug repurposing studies employ various approaches and methodologies to identify potential new uses for existing drugs. Computational approaches involve data mining, bioinformatics, and network analysis to uncover drug-target interactions and identify potential candidates for repurposing. High-throughput screening assays can be employed to assess the activity of approved drugs against new targets or pathways. Phenotypic screening involves testing approved drugs on disease models or cell lines to identify potential therapeutic effects. Additionally, knowledge-driven approaches leverage existing scientific literature and databases to explore connections between diseases and drugs. These diverse methodologies, often used in combination, facilitate the identification of repurposed drugs with potential efficacy in specific diseases like COPD [10].

### **Repurposed drugs with potential therapeutic benefits in COPD**

#### **Clinical studies for COPD management**

Several repurposed drugs have shown promise in preclinical and clinical studies for COPD management. For example, the macrolide antibiotic azithromycin has exhibited anti-inflammatory and immunomodulatory effects, reducing exacerbations and improving quality of life in COPD patients. Theophylline, traditionally used for asthma, has demonstrated bronchodilatory and anti-inflammatory properties in COPD. Statins, commonly prescribed for cardiovascular conditions, have shown potential in reducing inflammation and improving lung function. N-acetylcysteine, an antioxidant and mucolytic agent, has demonstrated benefits in reducing exacerbations and improving symptoms. These repurposed drugs offer potential alternatives or adjuncts to existing therapies for COPD management [11].

## **Classification of Repurposed Drugs Based on Their Mechanisms of Action**

Repurposed drugs for COPD can be classified based on their mechanisms of action into several categories. Bronchodilators, such as beta-agonists and anticholinergics, act on airway smooth muscles to relax and improve airflow. Anti-inflammatory agents, including corticosteroids and phosphodiesterase-4 inhibitors, target the inflammatory response in the lungs, reducing airway inflammation and exacerbations. Mucolytic agents, like N-acetylcysteine, promote mucus clearance and reduce mucus hypersecretion. Antioxidants, such as statins and N-acetylcysteine, combat oxidative stress and mitigate lung damage. Immunomodulatory drugs, such as macrolide antibiotics, modulate immune responses and reduce exacerbation rates. Each class of repurposed drugs offers a unique mechanism of action in COPD management [12].

### **Safety and efficacy considerations**

#### **Assessment of safety profiles and potential side effects associated with repurposed drugs in COPD**

Assessing the safety profiles and potential side effects of repurposed drugs in COPD is crucial for their clinical use. While repurposed drugs have already undergone safety evaluations for their original indications, it is essential to consider specific concerns in the context of COPD [13]. Common side effects may include gastrointestinal disturbances, cardiovascular effects, hepatic or renal toxicity, and interactions with other medications. Long-term use of certain repurposed drugs may also necessitate monitoring for potential adverse effects. Conducting well-designed clinical trials and post-marketing surveillance allows for a comprehensive evaluation of the safety profiles, enabling healthcare professionals to make informed decisions regarding the use of repurposed drugs in COPD patients [14][15].

#### **Evaluation of Efficacy Outcomes and Clinical Evidence Supporting the Use of Repurposed Drugs in COPD Treatment**

The evaluation of efficacy outcomes and clinical evidence supporting the use of repurposed drugs in COPD treatment involves analyzing data from preclinical studies, randomized controlled trials

(RCTs), and real-world studies. Efficacy outcomes may include improvements in lung function, reduction in exacerbations, symptom relief, and improvements in quality of life. Clinical evidence for repurposed drugs in COPD treatment is derived from RCTs comparing the drug of interest to placebo or standard therapy, as well as real-world studies assessing its effectiveness in routine clinical practice. Well-designed studies with appropriate sample sizes, rigorous methodology, and clinically meaningful endpoints are essential for establishing the efficacy and potential benefits of repurposed drugs in COPD management [16].

### **Future Directions and Challenges**

#### **Identification of potential barriers and challenges in the successful implementation of repurposed drugs in COPD management**

The successful implementation of repurposed drugs in COPD management may face several barriers and challenges. Firstly, regulatory considerations can pose challenges, as repurposed drugs may require additional approvals or modifications to their existing labeling for use in COPD. Ensuring adequate reimbursement and coverage by healthcare systems and insurance providers is another hurdle for widespread access to repurposed drugs [17].

Another challenge is the need for robust clinical evidence supporting the efficacy and safety of repurposed drugs in COPD. Conducting well-designed clinical trials specifically targeting COPD patients can be time-consuming and resource-intensive. Additionally, the heterogeneity of COPD and variations in patient responses to repurposed drugs pose challenges in identifying subpopulations that would benefit the most. Drug availability and cost may also impact implementation. Some repurposed drugs may not be readily available or affordable in certain regions or healthcare systems, limiting their accessibility to COPD patients. Furthermore, physician awareness and adoption of repurposed drugs may be a barrier, as physicians may be more familiar with and inclined to prescribe established therapies rather than considering repurposed options [18][19].

Patient acceptance and adherence can also be challenging. Patients may be hesitant to try repurposed drugs due to unfamiliarity or

concerns about potential side effects. Complex dosing regimens or differences in administration methods compared to standard COPD therapies may affect patient adherence. Addressing these barriers requires collaboration between regulatory agencies, healthcare systems, researchers, and patient advocacy groups. Conducting well-designed trials, raising awareness among physicians, ensuring affordability and accessibility, and providing patient education are essential steps in overcoming these challenges and successfully implementing repurposed drugs in COPD management [20].

## DISCUSSION

The comprehensive review on drug repurposing in COPD underscores the critical need to broaden therapeutic options for disease management. Through the exploration of repurposing existing drugs, the review emphasizes the potential benefits and advantages of this approach in COPD treatment. The discussion section of the review addresses several key points.

Firstly, it delves into the limitations and challenges associated with existing therapies in COPD, emphasizing the urgent need for alternative treatment options that can offer improved outcomes for patients. The review further discusses the rationale for exploring repurposed drugs in COPD management, highlighting the complex pathophysiology of COPD and how repurposed drugs can target specific mechanisms, providing potential benefits beyond existing treatments.

Additionally, the review examines various approaches and methodologies used in drug repurposing studies, emphasizing the importance of computational approaches, high-throughput screening assays, and phenotypic screening in identifying potential repurposed drugs. The evaluation of safety profiles and potential side effects associated with repurposed drugs in COPD is also discussed, emphasizing the need for careful assessment and monitoring to ensure patient safety during the use of repurposed drugs.

Moreover, the review evaluates the clinical evidence supporting the use of repurposed drugs in COPD treatment, emphasizing the importance of well-designed studies, including RCTs and real-

world studies, to establish the efficacy and potential benefits of repurposed drugs.

The discussion concludes by identifying potential barriers and challenges in the successful implementation of repurposed drugs in COPD management, including regulatory considerations, reimbursement issues, clinical evidence requirements, drug availability, physician awareness, and patient acceptance and adherence. Finally, the review explores future research directions and areas of exploration in drug repurposing for COPD. It highlights the significance of targeting specific molecular pathways, personalized medicine approaches, combination therapies, and novel drug delivery systems. It also emphasizes the importance of long-term safety and efficacy assessments, biomarker discovery, and the potential of combining repurposed drugs with novel agents.

## CONCLUSION

In conclusion, drug repurposing presents a promising approach to expanding therapeutic options for COPD management. The comprehensive review underscores the need for alternative treatments to address the limitations of current therapies. By repurposing existing drugs, the known safety profiles can be leveraged, accelerating their availability and potentially targeting specific mechanisms involved in COPD pathogenesis. The review emphasizes the importance of evaluating safety profiles, efficacy outcomes, and clinical evidence supporting repurposed drugs in COPD. Well-designed studies, including RCTs and real-world studies, are essential for establishing the benefits and risks of repurposed drugs for COPD patients.

While challenges such as regulatory considerations, reimbursement issues, and physician and patient acceptance exist, future research directions hold promise. Exploring specific molecular pathways, personalized medicine approaches, combination therapies, and novel drug delivery systems can enhance the effectiveness of repurposed drugs in COPD treatment. Overall, this comprehensive review underscores the potential of drug repurposing in COPD, urging further research and collaboration among stakeholders. By expanding therapeutic options, improvements in disease management, enhanced patient outcomes, and alleviation of the

global burden of COPD can be achieved. Continued efforts in this field have the potential to revolutionize COPD treatment and improve the lives of millions affected by this chronic respiratory condition.

### Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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