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**Strengthening pharmacotherapy research for COVID-19-induced pulmonary fibrosis**

Liu YM *et al.* Research pharmacotherapy for COVID-19-induced PF

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**Abstract**

The global spread of severe acute respiratory syndrome coronavirus 2 has resulted in a significant number of individuals developing pulmonary fibrosis (PF), an irreversible lung injury. This condition can manifest within a short interval following the onset of pneumonia symptoms, sometimes even within a few days. While lung transplantation is a potentially lifesaving procedure, its limited availability, high costs, intricate surgeries, and risk of immunological rejection present significant drawbacks. The optimal timing of medication administration for coronavirus disease 2019 (COVID-19)-induced PF remains controversial. Despite this, it is crucial to explore pharmacotherapy interventions, involving early and preventative treatment as well as pharmacotherapy options for advanced-stage PF. Additionally, studies have demonstrated disparities in anti-fibrotic treatment based on race and gender factors. Genetic mutations may also impact therapeutic efficacy. Enhancing research efforts on pharmacotherapy interventions, while considering relevant pharmacological factors and optimizing the timing and dosage of medication administration, will lead to enhanced, personalized, and fair treatment for individuals impacted by COVID-19-related PF. These measures are crucial in lessening the burden of the disease on healthcare systems and improving patients' quality of life.

**Key Words:** COVID-19; Pulmonary fibrosis; Pharmacotherapy intervention; Medication administration; Timing; Dosage

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**Core Tip:** Pulmonary fibrosis (PF) induced by coronavirus disease 2019 (COVID-19) represents a significant and serious complication of the disease. When PF advances to a critical stage, lung transplantation becomes the sole life-saving option. Our call is for an intensified focus on researching pharmacotherapy interventions for COVID-19-induced PF, aimed at identifying potential medication options.

**INTRODUCTION**

Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by the severe acute respiratory syndrome coronavirus 2. It has been observed that COVID-19 patients may develop pulmonary fibrosis (PF), a serious complication that affects their quality of life even after recovery[1]. PF is characterized by damage to the lung tissue, excessive scarring, and impaired lung function[2]. This often leads to respiratory failure and can be fatal[3]. It is important to explore pharmacotherapy interventions that can prevent or reduce fibrosis damage in COVID-19 patients[4].

**PATHOGENESIS OF COVID-19-INDUCED PF**

The pathogenesis of COVID-19-induced PF is complex and involves various molecular mechanisms. Transforming growth factor-β and PI3K/AKT signaling pathways play important roles in the development of PF[5]. The activation of these pathways leads to fibroblast proliferation, migration, and conversion into myofibroblasts, resulting in excessive scarring[6]. Cytokine storm, characterized by an overactive immune response, also contributes to the activation, proliferation, and migration of fibroblasts[7]. Additionally, the EGFR pathway has been implicated in COVID-19-related PF[8].

**PHARMACOTHERAPY INTERVENTIONS**

***Medication commonly used in clinical treatment***

Pirfenidone and nintedanib are currently approved for the treatment of idiopathic PF and have shown efficacy in COVID-19-induced PF[4,9-11]. Pirfenidone inhibits fibroblast proliferation and extracellular matrix deposition, while nintedanib slows down the development of fibrosis[6,10]. Both medications have similar efficacy in reducing lung function decline[12,13]. However, pirfenidone may cause liver injury, and nintedanib is not recommended for patients with moderate or severe liver injury[14,15].

***Medications less commonly used in clinical treatment***

N-acetylcysteine (NAC) and mesenchymal stem cell (MSC) therapy have shown potential as adjuvant treatments for COVID-19-induced PF. NAC replenishes glutathione levels and MSCs have anti-inflammatory and regenerative properties[16,17]. DPP-4 inhibitors and statins, commonly used for diabetes and cholesterol management, respectively, may also prevent fibrosis[7,18]. Anakinra, Xuanfei Baidu Decoction (a traditional Chinese medicine), nimotuzumab, and vitamin D supplementation have shown promising results in treating COVID-19-induced PF[19-22].

***Potential medication therapies with limited evidence***

Several medications, such as natural polysaccharides, baicalin, the endocannabinoid system, dihydroartemisinin and (-)-Epigallocatechin-3-gallate, have shown anti-fibrotic effects in preclinical trials but lack clinical trial date[23-27]. Tocilizumab and baricitinib combination therapy has shown effectiveness but has controversial safety concerns[21,28]. PI3K inhibitors hold promise but require further exploration for safe use[29].

**PHARMACOLOGICAL CONSIDERATIONS ON ANTI-FIBROSIS TREATMENT FOR COVID-19-INDUCED PF**

When testing the effects of pharmacotherapy for COVID-19-induced PF, it is crucial to consider pharmacological factors. Studies have demonstrated that nintedanib exhibits comparable therapeutic effects across various ethnic groups, including Asian and White patients[15,30]. Additionally, the literature finding also confirms that the gender has no noticeable effect on nintedanib pharmacokinetics[15]. In terms of the utilization of anti-fibrotic treatment, Black patients are 40% less likely than their White counterparts to receive such treatment, and similarly, female patients are 59% less likely than their male counterparts[31].

These findings offer valuable insights into potential disparities in the administration of anti-fibrotic treatment, highlighting the importance and potential significance of race and gender factors. Further research in this area holds great promise for exploring and understanding these disparities in greater detail, which can contribute to the development of more personalized and equitable treatment approaches. Additionally, investigating the influence of race and gender on the effectiveness and safety profiles of anti-fibrotic therapies can provide a deeper understanding of their impact on different patient populations, ultimately leading to improved healthcare outcomes for all individuals.

In individuals with telomerase reverse transcriptase (TERT) mutations, there may be an increased risk of developing COVID-19-induced PF[32]. It has also been observed that TERT/TERC mutations are resistant to pirfenidone therapy[33]. Additionally, other genetic variants such as MUC5B, DPP9, and ATP11A have been associated with COVID-19-induced PF[34]. Exploring the role of genetics in this condition may pave the way for the development of novel agents for targeted therapy and personalized treatment.

**TIMING AND DOSAGES OF MEDICATIONS PROPOSED FOR COVID-19-INDUCED PF**

The optimal timing of medication administration for COVID-19-induced PF remains a topic of ongoing debate, with advocates for early and preventative approaches as well as those in favor of using anti-fibrotic drugs only when clear signs of PF with progressive exacerbations are present[7,10,35]. Each perspective is grounded in its own reasoning. Supporters of early intervention argue that COVID-19-induced PF might constitute an irreversible process, while those who are cautious about early treatment weigh the cost of anti-fibrosis treatment against the potential inevitability of COVID-19-induced PF. The nuances of these contrasting views underscore the complexity surrounding the optimal timing for administering anti-fibrotic drugs in the context of COVID-19-related complications. Further research on the timing of anti-fibrotic medication for PF caused by COVID-19 from both basic and clinical perspectives is necessary.

In order to achieve successful pharmacotherapy, proper dosages of promising drugs for anti-fibrosis treatment should be investigated. Table 1 summarizes the recommended dosages for some medications currently in use. Additionally, the development of novel drug delivery systems, such as inhalable systems including lipid-based nanocarriers, nanovesicles, polymeric nanocarriers, protein nanocarriers, nanosuspensions, nanoparticles, gold nanoparticles, and hydrogel, could prove to be a promising area for the treatment of PF caused by COVID-19[36].

**CONCLUSION**

COVID-19-induced PF has emerged as a challenging problem with no known cure. Pharmacotherapy interventions aimed at delaying disease progression and improving quality of life are crucial. Pirfenidone and nintedanib are currently the mainstay of treatment, while other medications serve as potential adjuvant therapies. Rational use of DPP-4 inhibitors, statins, NAC, anakinra, vitamin D, and nimotuzumab may prevent or control the progression of COVID-19-induced PF. Traditional Chinese medicine and other experimental medications require further research and clinical trials to evaluate their efficacy and safety. Additional research is necessary to strengthen pharmacotherapy interventions aimed at managing COVID-19-induced PF, while taking into account relevant pharmacological factors and optimizing the timing and dosage of medication administration. Such efforts will lead to the development of enhanced, equitable, and personalized approaches to managing this condition.

**REFERENCES**

1 **Wang J**, Wang BJ, Yang JC, Wang MY, Chen C, Luo GX, He WF. [Research advances in the mechanism of pulmonary fibrosis induced by coronavirus disease 2019 and the corresponding therapeutic measures]. *Zhonghua Shao Shang Za Zhi* 2020; **36**: 691-697 [PMID: 32174095 DOI: 10.3760/cma.j.cn501120-20200307-00132]

2 **Zhan X**, Liu B, Tong ZH. [Postinflammatroy pulmonary fibrosis of COVID-19: the current status and perspective]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020; **43**: 728-732 [PMID: 32894907 DOI: 10.3760/cma.j.cn112147-20200317-00359]

3 **George PM**, Patterson CM, Reed AK, Thillai M. Lung transplantation for idiopathic pulmonary fibrosis. *Lancet Respir Med* 2019; **7**: 271-282 [PMID: 30738856 DOI: 10.1016/S2213-2600(18)30502-2]

4 **Ferrara F**, Granata G, Pelliccia C, La Porta R, Vitiello A. The added value of pirfenidone to fight inflammation and fibrotic state induced by SARS-CoV-2: Anti-inflammatory and anti-fibrotic therapy could solve the lung complications of the infection? *Eur J Clin Pharmacol* 2020; **76**: 1615-1618 [PMID: 32594204 DOI: 10.1007/s00228-020-02947-4]

5 **Wu N**, Li Z, Wang J, Geng L, Yue Y, Deng Z, Wang Q, Zhang Q. Low molecular weight fucoidan attenuating pulmonary fibrosis by relieving inflammatory reaction and progression of epithelial-mesenchymal transition. *Carbohydr Polym* 2021; **273**: 118567 [PMID: 34560978 DOI: 10.1016/j.carbpol.2021.118567]

6 **Al-Kuraishy HM**, Batiha GE, Faidah H, Al-Gareeb AI, Saad HM, Simal-Gandara J. Pirfenidone and post-Covid-19 pulmonary fibrosis: invoked again for realistic goals. *Inflammopharmacology* 2022; **30**: 2017-2026 [PMID: 36044102 DOI: 10.1007/s10787-022-01027-6]

7 **Smelcerovic A**, Kocic G, Gajic M, Tomovic K, Djordjevic V, Stankovic-Djordjevic D, Anderluh M. DPP-4 Inhibitors in the Prevention/Treatment of Pulmonary Fibrosis, Heart and Kidney Injury Caused by COVID-19-A Therapeutic Approach of Choice in Type 2 Diabetic Patients? *Front Pharmacol* 2020; **11**: 1185 [PMID: 32848788 DOI: 10.3389/fphar.2020.01185]

8 **Abdo Cuza AA**, Ávila JP, Martínez RM, González JJ, Aspuro GP, Gutiérrez Martínez JA, Suzarte MR, Hernández DS, Añé-Kouri AL, Ramos TC. Nimotuzumab for COVID-19: case series. *Immunotherapy* 2021 [PMID: 34806405 DOI: 10.2217/imt-2021-0269]

9 **Medical Panel of Severe/Critical COVID-19,** The Third Affiliated Hospital of Sun Yat-sen University. Management of severe/critical novel COVID-19: recommendations of the third affiliated hospital of Sun Yat-sen University. *Zhongshan Daxue Xuebao* 2020; **41**: 345351

10 **Hashemian SM**, Farhadi T, Varahram M, Velayati AA. Nintedanib: a review of the properties, function, and usefulness to minimize COVID-19-induced lung injury. *Expert Rev Anti Infect Ther* 2023; **21**: 7-14 [PMID: 36440472 DOI: 10.1080/14787210.2023.2153116]

11 **Choudhary R**, Kumar A, Ali O, Pervez A. Effectiveness and Safety of Pirfenidone and Nintedanib for Pulmonary Fibrosis in COVID-19-Induced Severe Pneumonia: An Interventional Study. *Cureus* 2022; **14**: e29435 [PMID: 36299940 DOI: 10.7759/cureus.29435]

12 **Vancheri C**, Kreuter M, Richeldi L, Ryerson CJ, Valeyre D, Grutters JC, Wiebe S, Stansen W, Quaresma M, Stowasser S, Wuyts WA; INJOURNEY Trial Investigators. Nintedanib with Add-on Pirfenidone in Idiopathic Pulmonary Fibrosis. Results of the INJOURNEY Trial. *Am J Respir Crit Care Med* 2018; **197**: 356-363 [PMID: 28889759 DOI: 10.1164/rccm.201706-1301OC]

13 **George PM**, Wells AU, Jenkins RG. Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy. *Lancet Respir Med* 2020; **8**: 807-815 [PMID: 32422178 DOI: 10.1016/S2213-2600(20)30225-3]

14 **Sakızcı Uyar B**, Ensarioğlu K, Kurt EB, Özkan D, Özbal Güneş S. Anti-fibrotic Treatment for Pulmonary Fibrosis Induced by COVID-19: A Case Presentation. *Turk J Anaesthesiol Reanim* 2022; **50**: 228-231 [PMID: 35801331 DOI: 10.5152/TJAR.2021.20450]

15 **Wind S**, Schmid U, Freiwald M, Marzin K, Lotz R, Ebner T, Stopfer P, Dallinger C. Clinical Pharmacokinetics and Pharmacodynamics of Nintedanib. *Clin Pharmacokinet* 2019; **58**: 1131-1147 [PMID: 31016670 DOI: 10.1007/s40262-019-00766-0]

16 **Micheletto C**, Izquierdo JL, Avdeev SN, Rada Escobar RA, Pacheco Gallego MC. N-acetylcysteine as a therapeutic approach to post-COVID-19 pulmonary fibrosis adjunctive treatment. *Eur Rev Med Pharmacol Sci* 2022; **26**: 4872-4880 [PMID: 35856379 DOI: 10.26355/eurrev\_202207\_29212]

17 **Chen L**, Qu J, Kalyani FS, Zhang Q, Fan L, Fang Y, Li Y, Xiang C. Mesenchymal stem cell-based treatments for COVID-19: status and future perspectives for clinical applications. *Cell Mol Life Sci* 2022; **79**: 142 [PMID: 35187617 DOI: 10.1007/s00018-021-04096-y]

18 **Sadeghdoust M**, Aligolighasemabadi F, Dehesh T, Taefehshokr N, Sadeghdoust A, Kotfis K, Hashemiattar A, Ravandi A, Aligolighasemabadi N, Vakili O, Grabarek B, Staszkiewicz R, Łos MJ, Mokarram P, Ghavami S. The Effects of Statins on Respiratory Symptoms and Pulmonary Fibrosis in COVID-19 Patients with Diabetes Mellitus: A Longitudinal Multicenter Study. *Arch Immunol Ther Exp (Warsz)* 2023; **71**: 8 [PMID: 36853269 DOI: 10.1007/s00005-023-00672-1]

19 **Nan D**, Abraira-Meriel C, de la Roz-Fernández S, Maestre-Orozco T, Hernandez JL, Fernandez-Ayala M. Delayed Use of the Recombinant Human IL-1 Receptor Antagonist Anakinra in Five COVID-19 Patients with Pulmonary Fibrosis and Persistent Hypoxaemia: A Preliminary Report. *Eur J Case Rep Intern Med* 2021; **8**: 002821 [PMID: 34790623 DOI: 10.12890/2021\_002821]

20 **Wang Y**, Sang X, Shao R, Qin H, Chen X, Xue Z, Li L, Wang Y, Zhu Y, Chang Y, Gao X, Zhang B, Zhang H, Yang J. Xuanfei Baidu Decoction protects against macrophages induced inflammation and pulmonary fibrosis via inhibiting IL-6/STAT3 signaling pathway. *J Ethnopharmacol* 2022; **283**: 114701 [PMID: 34606948 DOI: 10.1016/j.jep.2021.114701]

21 **Londres HD**, Armada JJ, Martínez AH, Abdo Cuza AA, Sánchez YH, Rodríguez AG, Figueroa SS, Llanez Gregorich EM, Torres Lahera ML, Peire FG, González TM, González YZ, Añé Kouri AL, Palomo AG, Concepción MT, Pérez LM, Luaces-Alvarez PL, Iglesias DE, Hernández DS, Suzarte MR, Ramos TC. Blocking EGFR with nimotuzumab: a novel strategy for COVID-19 treatment. *Immunotherapy* 2022; **14**: 521-530 [PMID: 35306855 DOI: 10.2217/imt-2022-0027]

22 **Cutolo M**, Paolino S, Smith V. Evidences for a protective role of vitamin D in COVID-19. *RMD Open* 2020; **6** [PMID: 33372031 DOI: 10.1136/rmdopen-2020-001454]

23 **Chen RR**, Li YJ, Chen JJ, Lu CL. A review for natural polysaccharides with anti-pulmonary fibrosis properties, which may benefit to patients infected by 2019-nCoV. *Carbohydr Polym* 2020; **247**: 116740 [PMID: 32829859 DOI: 10.1016/j.carbpol.2020.116740]

24 **Song S**, Ding L, Liu G, Chen T, Zhao M, Li X, Li M, Qi H, Chen J, Wang Z, Wang Y, Ma J, Wang Q, Li X, Wang Z. The protective effects of baicalin for respiratory diseases: an update and future perspectives. *Front Pharmacol* 2023; **14**: 1129817 [PMID: 37007037 DOI: 10.3389/fphar.2023.1129817]

25 **Lucaciu O**, Aghiorghiesei O, Petrescu NB, Mirica IC, Benea HRC, Apostu D. In quest of a new therapeutic approach in COVID-19: the endocannabinoid system. *Drug Metab Rev* 2021; **53**: 478-490 [PMID: 33683968 DOI: 10.1080/03602532.2021.1895204]

26 **You X**, Jiang X, Zhang C, Jiang K, Zhao X, Guo T, Zhu X, Bao J, Dou H. Dihydroartemisinin attenuates pulmonary inflammation and fibrosis in rats by suppressing JAK2/STAT3 signaling. *Aging (Albany NY)* 2022; **14**: 1110-1127 [PMID: 35120332 DOI: 10.18632/aging.203874]

27 **Liu J**, Bodnar BH, Meng F, Khan AI, Wang X, Saribas S, Wang T, Lohani SC, Wang P, Wei Z, Luo J, Zhou L, Wu J, Luo G, Li Q, Hu W, Ho W. Epigallocatechin gallate from green tea effectively blocks infection of SARS-CoV-2 and new variants by inhibiting spike binding to ACE2 receptor. *Cell Biosci* 2021; **11**: 168 [PMID: 34461999 DOI: 10.1186/s13578-021-00680-8]

28 **Kai Y**, Matsuda M, Suzuki K, Kasamatsu T, Kajita A, Uno K, Muro S. Tocilizumab and Baricitinib for Recovery From Acute Exacerbation of Combined Pulmonary Fibrosis and Emphysema Secondary to COVID-19 Infection: A Case Report. *Cureus* 2022; **14**: e23411 [PMID: 35481309 DOI: 10.7759/cureus.23411]

29 **Margaria JP**, Moretta L, Alves-Filho JC, Hirsch E. PI3K Signaling in Mechanisms and Treatments of Pulmonary Fibrosis Following Sepsis and Acute Lung Injury. *Biomedicines* 2022; **10** [PMID: 35453505 DOI: 10.3390/biomedicines10040756]

30 **Taniguchi H**, Xu Z, Azuma A, Inoue Y, Li H, Fujimoto T, Bailes Z, Schlenker-Herceg R, Kim DS. Subgroup analysis of Asian patients in the INPULSIS(®) trials of nintedanib in idiopathic pulmonary fibrosis. *Respirology* 2016; **21**: 1425-1430 [PMID: 27399197 DOI: 10.1111/resp.12852]

31 **Kaul B**, Lee JS, Petersen LA, McCulloch C, Rosas IO, Bandi VD, Zhang N, DeDent AM, Collard HR, Whooley MA. Disparities in Antifibrotic Medication Utilization Among Veterans With Idiopathic Pulmonary Fibrosis. *Chest* 2023; **164**: 441-449 [PMID: 36801465 DOI: 10.1016/j.chest.2023.02.027]

32 **Yetkin NA**, Kiraz A, Baran Ketencioğlu B, Bol C, Tutar N. Are MUC5B and TERT mutations genetic risk factors for pulmonary fibrosis in individuals with severe COVID-19? *Tuberk Toraks* 2023; **71**: 34-40 [PMID: 36912407 DOI: 10.5578/tt.20239905]

33 **Ma H**, Wu X, Li Y, Xia Y. Research Progress in the Molecular Mechanisms, Therapeutic Targets, and Drug Development of Idiopathic Pulmonary Fibrosis. *Front Pharmacol* 2022; **13**: 963054 [PMID: 35935869 DOI: 10.3389/fphar.2022.963054]

34 **Patrucco F**, Solidoro P, Gavelli F, Apostolo D, Bellan M. Idiopathic Pulmonary Fibrosis and Post-COVID-19 Lung Fibrosis: Links and Risks. *Microorganisms* 2023; **11** [PMID: 37110318 DOI: 10.3390/microorganisms11040895]

35 **Chinese Research Hospital Association**; Respiratory Council. [Expert recommendations for the diagnosis and treatment of interstitial lung disease caused by novel coronavirus pneumonia]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020; **43**: 827-833 [PMID: 32992435 DOI: 10.3760/cma.j.cn112147-20200326-00419]

36 **Wan Q**, Zhang X, Zhou D, Xie R, Cai Y, Zhang K, Sun X. Inhaled nano-based therapeutics for pulmonary fibrosis: recent advances and future prospects. *J Nanobiotechnology* 2023; **21**: 215 [PMID: 37422665 DOI: 10.1186/s12951-023-01971-7]

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**Table 1 The recommended dosages in literatures for some medications in use**

|  |  |
| --- | --- |
| **Medications** | **Recommended dosages** |
| Pirfenidone | 2400 mg/d for 12-24 wk[6] |
| Nintedanib | 150 mg or 100 mg (for patients with mild hepatic impairment) twice daily[10] |
| N-acetylcysteine | Oral 600 mg every 8 h, oral 600 mg twice daily for 14 d, or intravenous 40 mg/(kg × d) for 3 d[16] |
| Anakinra | A total dose of 600 mg (a loading dose of 200 mg twice daily, followed by 100 mg once daily for 2 d)[19] |
| Nimotuzumab | Intravenous administration: 2-3 times with an interval of 72 h, including a loading dose of 200 mg, followed by 100 mg[21] |
| Vitamin D | COVID-19 patients with 25-hydrodroxyvitamin D serum levels under 20 ng/mL: 6000-7000 oral IU/d for the first 6-8 wk for correction of deficiency and 2000 to 3000 oral IU/d for maintenance[22] |

COVID-19: Coronavirus disease 2019.