

ORIGINAL ARTICLE

Preventive Effect of Turmeric against Anti-Mosquito Smoke Induced Pulmonary Fibrosis in Laboratory Rat

Saira Jawed,¹ Wafa Omer²

ABSTRACT

Objective: To appraise the preventive effect of turmeric on anti-mosquito coil smoke induced interstitial fibrosis in lungs of Sprague Dawley rats.

Study Design: Randomized control trial.

Place and Duration of Study: This study was completed in 10 months from 1st August 2014 to 28th May 2015; conducted at Islamic International Medical College, Rawalpindi and National Institute of Health (NIH), Islamabad, Pakistan.

Material and Methods: Three equal groups of 21 adult albino rats were made. Control Group X was retained in fresh air. Experimental Groups M & T inhaled Mosquito Coil smoke for 12 weeks. Group T also had oral turmeric 300mg/kg body weight. After 12 weeks rats were dissected, and their lung tissues were studied microscopically for the presence of fibrosis.

Results: Interstitial Fibrosis was markedly present in the histological sections of lung tissues from experimental group M showing thickened fibrotic alveolar walls and inflammatory cell infiltrate with reduced air spaces in all animals (100%) in group M. Fibrosis was present in 2 out of 7 rats in group T showing a significant protection with only 28.5% of animals with fibrotic lungs. No interstitial fibrosis (0%) was seen in the lung tissues of animals in control group X; all 7 rats showed well-formed alveoli.

Conclusions: Interstitial lung fibrosis caused by Anti-Mosquito coil smoke can be protected with the use of turmeric.

Key Words: Covid-19, Curcuma, Mosquito Coil, Pulmonary Fibrosis, Turmeric.

Introduction

Modern medicine to a large extent has failed in its ambition to control both acute and chronic diseases. Traditional herbal medicines have been found effective for the treatment and prevention of several diseases. Turmeric is a traditional herbal medicine.¹ It's broad reaching mechanism of action and lack of systemic toxicity may make it best suited as an adjuvant therapy for various viral and other respiratory disorders like tobacco smoke induced epithelial damage and acute lung injury that are resistant to currently available therapies.² Several diseases have been found to have inflammatory origin. Turmeric is safe, affordable and efficacious

nutraceutical. Turmeric has significant anti-inflammatory and anti-oxidant properties.³ It has gained value as a digestive aid, treatment for fever, wounds, infections and blood disorders. Data from animal and pharmacological studies also supports that active ingredients in turmeric play a protective role in various diseases like acute respiratory distress syndrome, chronic obstructive pulmonary disease and allergic asthma and also have proven antiviral properties against para-influenza type 3, respiratory syncytial virus and herpes simplex virus,^{4,5,6} its therapeutic action is based on the inflection or prevention of oxidative stress and inflammation confirmed with the studies done at molecular & cellular levels.^{7,8} The findings in these researches give substance to the possibility of testing turmeric for the prevention of pulmonary fibrosis caused by allethrins released from burning anti-mosquito coils. Mosquitoes and the transmission of the mosquito borne diseases have been historically controlled by the use of chemical insecticides and mosquito repelling agents like anti-mosquito coil containing Pyrethroids (allethrins), which play a central role in

Department of Anatomy¹/Pathology²

HBS Medical and Dental College, Islamabad

Correspondence:

Dr. Saira Jawed

Assistant Professor

Department of Anatomy

HBS Medical and Dental College, Islamabad

E-mail: sairajawed371@gmail.com

Funding Source: NIL; Conflict of Interest: NIL

Received: February 11, 2020; Revised: October 01, 2020

Accepted: October 10, 2020

mosquito control programs.⁹ More toxic products having higher concentration of allethrin are predominating the market due to the rapid spread of resistance worldwide.¹⁰ The use of allethrin in higher concentrations and a complicated mixture of metallic vapors to tackle the resistant mosquitoes, exposes the consumer to a severe health risk.¹¹ It has already been addressed in the literature that exposure to mosquito coil smoke can have toxic effects on the lungs and can induce histopathological changes like severe emphysema, hyperplasia, chronic obstructive pulmonary disease, edema, hemorrhage & fibrosis, necrosis, hyperemia, connective tissue infiltration by inflammatory cells and obstruction by hyaline material within the lung tissue.^{12,13}

The objective of the current research was to demonstrate the efficacy of turmeric in preventing pulmonary fibrosis as there is insufficient literature on the preventive characteristics of turmeric against anti-mosquito allethrin present in coil smoke.

Material and Methods

This randomized control trial conducted at Islamic International Medical College, Rawalpindi and National Institute of Health (NIH), Islamabad and was completed in 10 months. A total of 21 Sprague Dawley male rats weighing 250-300g were purchased from the animal house of National Institute of Health (NIH) Islamabad and were randomly divided into three groups; control group X and experimental groups M & T. The study was performed after an ethical approval from the Institutional Review Committee of Riphah International University. Female rats and the rats having a weight of less than 250 g or having a physical disability were excluded from the study. Groups M & T rats were placed in smoke exposure cabins at a temperature of 27±3°C with a 12hr light/dark cycle along with standard laboratory diet and water. Experimental groups were exposed to mosquito coil smoke for 7 hours per day for 12 weeks; group T received 300mg/kg body weight oral turmeric as well. All rats were sacrificed at the end of 12 weeks and left lungs of all were dissected out and preserved in 10% formalin. After tissue processing slides were prepared and stained with Masson's Trichrome to be studied microscopically first at low power, x10, and then at high power, x40 objective. The histological

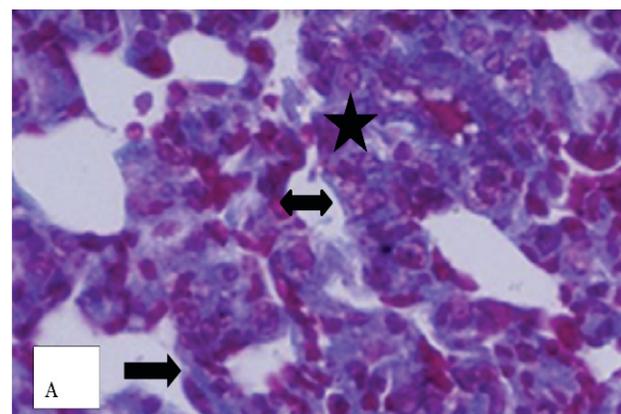
slides were interpreted by the pathologist. Slides were studied for presence of interstitial fibrosis. Masson's Trichrome stained collagen fibers causing thickening of alveolar septa & alveolar spaces filled with proteinaceous fluid and inflammatory cell infiltrate causing reduction in alveolar spaces was taken as a criterion for interstitial fibrosis.

Results

The lung tissue of all rats (100%) in group M (Fig 2A) had a Masson's trichrome stained dense fibrous connective tissue with collagen fibrils & thickening of alveolar walls with cellular infiltration, proliferation & airspaces filled with proteinaceous fluid. The interstitial infiltrate consisted of lymphocytes, plasma cells, mast cells and eosinophils resulting in interstitial fibrosis. Interstitial pulmonary fibrosis was present in 2 out of 7 rats in group T; thus rats in group T showed a remarkable protection from pulmonary fibrosis with only 28.5% of animals developing fibrosis (Fig 2B). The result is shown in table (Fig 1). The Masson's Trichrome stained histological slides from the rats in control group X had normal honeycomb like alveolar structure with well-formed alveolar walls (Fig 2C).

Table 1: Table representing percentage of interstitial lung fibrosis in control and Experimental Groups

Groups (Total rats 21 ; 7 rats in each group)	Interstitial fibrosis		Presence of fibrosis (percentage)
	Present	Absent	
Group X	0	7	0%
Group M	7	0	100%
Group T	2	5	28.5%



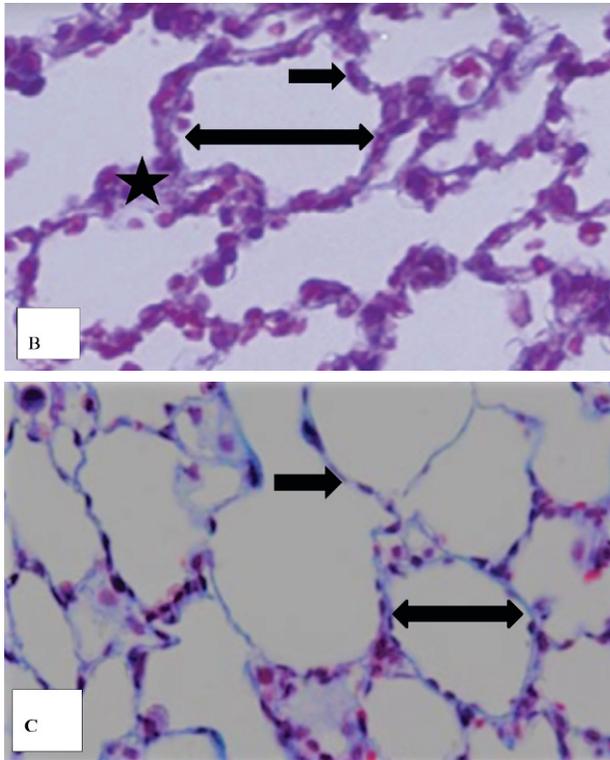


Fig 2: (A) Histological Section of a Rat Lung from Group M Showing Thickened Fibrotic Alveolar Septa (Arrow), Proteinaceous Fluid (Star) With Reduced Air Space (Double Headed Arrow)
(B) Histological Section of a Rat Lung from Group T Showing Less Thickened Alveolar Septa (Arrow) With A Few Cellular Infiltrates (Star), Well-Formed Alveoli and Preserved Air Space (Double Headed Arrow)
(C) Histological Section of A Rat Lung from Group X Showing Normal Alveolar Septa (Arrow) and Alveoli Showing Honeycomb Like Pattern (Double Headed Arrow)

Discussion

Pulmonary fibrosis is a pattern of reaction to parenchymal damage in which lung has unusually high collagen fiber content per unit volume of tissue.¹⁴ In the present study histological sections of the lungs of rats are stained with Masson's Trichrome in order to observe the fibrotic thickening of alveolar septa, reduced air spaces and presence of proteinaceous fluid. 100% of rats in Group M showed thickened alveolar walls & proteinaceous fluid accumulated in interstitial space along with interstitial fibrosis. In Group T, only 28.5% of rats showed the said histopathological parameters. Inflammation is one of the etiological factor for the development of fibrosis.¹⁴ As inflammatory reaction

is observed in this case, it can be correlated to the development of fibrosis. Fibrosis in the pulmonary interstitium is usually a result of alveolar damage due to physical, chemical or microbial agents.¹⁴ Allethrin in the coil smoke can be linked to the interstitial fibrosis observed in this study. The process of interstitial fibrosis is characterized by thickened alveolar walls that are fibrotic and contain an inflammatory cell infiltrate with reduced air spaces. Macrophages are thought to be responsible for expressing fibroblast growth factor, resulting in the proliferation of fibroblasts and subsequent development of fibrosis. The excessive deposition of collagen fibers reflects reduced lung capacity leading to respiratory distress which is the main effect of air pollutant exposure. Earlier study mentions that smoke induces lung destruction with inflammatory reaction, more fibroblasts are brought to the irritated area leading to more collagen fiber deposition.^{15,16} In another study, fibrotic change was observed in lung parenchyma of rats after 6 weeks of exposure to mosquito coil smoke. Similar histological appearance was seen in the lungs exposed to asbestos and cigarette smoke.¹⁷ Excessive deposition of collagen fiber has also been observed in the lungs of rats in similar inhalational studies.¹⁸ Turmeric is one of the herbal compounds that has been investigated in fibrosis research.^{19,20} In the present research only 28.5 % of histological sections of rat lungs in the Group T showed fibrous reaction. The result of this study is consistent with the previous studies. Turmeric administration can inhibit abnormal lung collagen formation.²¹ Turmeric supplementation suppresses alveolar macrophages, expression of fibroblast growth factor by the macrophages and other inflammatory cells thereby ameliorating the inflammatory responses in the lungs which prevents fibrosis in the lung tissue.²² The histopathological findings of the current research can further be utilized to test turmeric for the prophylaxis and treatment of Covid-19 induced pulmonary fibrosis; which is considered to be the most devastating outcome of this viral infection.²³

Conclusion

Interstitial lung fibrosis caused by anti-mosquito coil smoke can be protected with the use of turmeric.

REFERENCES

- Kant S, Lohiya A, Ahamed F, Abdulkader RS, Singh AK, Silan V. Comparative morbidity profile of patients attending an Ayurveda clinic and a modern medicine clinic of a primary health center in rural Haryana, India. *J Fam Med Prim care*. 2018;7(2):374.
- Liang Z, Wu R, Xie W, Zhu M, Xie C, Li X, et al. Curcumin reverses tobacco smoke-induced epithelial-mesenchymal transition by suppressing the MAPK pathway in the lungs of mice. *Mol Med Rep*. 2018;17(1):2019–25.
- Cheng K, Yang A, Hu X, Zhu D, Liu K. Curcumin attenuates pulmonary inflammation in lipopolysaccharide induced acute lung injury in neonatal rat model by activating peroxisome proliferator-activated receptor γ (PPAR γ) pathway. *Med Sci Monit Int Med J Exp Clin Res*. 2018;24:1178.
- Liu Z, Ying Y. The inhibitory effect of curcumin on virus-induced cytokine storm and its potential use in the associated severe pneumonia. *Front cell Dev Biol*. 2020;8:479.
- Akbik D, Ghadiri M, Chrzanowski W, Rohanzadeh R. Curcumin as a wound healing agent. *Life Sci [Internet]*. 2014;116(1):1–7. Available from: <http://dx.doi.org/10.1016/j.lfs.2014.08.016>.
- Lal J. Turmeric, curcumin and our life: a review. *Bull Env Pharmacol Life Sci*. 2012;1(7):11–7.
- Patel SS, Acharya A, Ray RS, Agrawal R, Raghuwanshi R, Jain P. Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. *Crit Rev Food Sci Nutr*. 2020;60(6):887–939.
- Salehi B, Stojanović-Radić Z, Matejić J, Sharifi-Rad M, Kumar NVA, Martins N, et al. The therapeutic potential of curcumin: A review of clinical trials. *Eur J Med Chem*. 2019;163:527–45.
- Mendis K, Rietveld A, Warsame M, Bosman A, Greenwood B, Wernsdorfer WH. From malaria control to eradication: The WHO perspective. *Trop Med Int Heal*. 2009;14(7):802–9.
- Karunaratne S, de Silva W, Weeraratne TC, Surendran SN. Insecticide resistance in mosquitoes: development, mechanisms and monitoring. *Ceylon J Sci*. 2018;47(4):299–309.
- Xiao Y, Murray J, Lenzen M. International trade linked with disease burden from airborne particulate pollution. *Resour Conserv Recycl*. 2018;129:1–11.
- Mohanta MK, Hasi AS, Haque MF, Saha AK. Supplementation of Vitamin A and C can effectively recover the Histological and Haematological Alteration caused by Mosquito Coil Smoke and Aerosol in Mice Model. *Int J Curr Microbiol App Sci*. 2019;8(5):2223–37.
- Naz M, Rehman N, Ansari MN, Kamal M, Ganaie MA, Awaad AS, et al. Comparative study of subchronic toxicities of mosquito repellents (coils, mats and liquids) on vital organs in Swiss albino mice. *Saudi Pharm J*. 2019;27(3):348–53.
- Riede U-N, Werner M. *Color Atlas of Pathology: Pathologic Principles, Associated Diseases, Sequelae*. Thieme; 2004.
- Roggli VL, Gibbs AR, Attanoos R, Churg A, Popper H, Cagle P, et al. Pathology of asbestosis—an update of the diagnostic criteria: report of the asbestosis committee of the college of american pathologists and pulmonary pathology society. *Arch Pathol Lab Med*. 2010;134(3):462–80.
- Wright JL, Churg A. Morphology of Small-airway Lesions in Patients with Asbestos Exposure. *Hum Pathol [Internet]*. 15(1):68–74. Available from: [http://dx.doi.org/10.1016/S0046-8177\(84\)80332-9](http://dx.doi.org/10.1016/S0046-8177(84)80332-9).
- Franks TJ, Galvin JR. Smoking-related “interstitial” lung disease. *Arch Pathol Lab Med*. 2014;139(8):974–7.
- Abdulla Al-Mamun M, Ataur Rahman M, Habibur Rahman M, Hoque KMF, Ferdousi Z, Matin MN, et al. Biochemical and histological alterations induced by the smoke of allethrin based mosquito coil on mice model. *BMC Clin Pathol [Internet]*. 2017 Aug;17(1):19. Available from: <https://doi.org/10.1186/s12907-017-0057-9>.
- Rheim FA, Ragab AA, Hammam F, El-Din Hamdy H, others. Protective Effects of Curcumin for Oxidative Stress and Histological Alterations Induced by Pyrethroid Insecticide in Albino Rats. *Egypt J Hosp Med*. 2015;31(1662):1–11.
- Wang L, Zheng X, Stevanovic S, Xiang Z, Liu J, Shi H, et al. Characterizing pollutant emissions from mosquito repellents incenses and implications in risk assessment of human health. *Chemosphere [Internet]*. 2018;191:962–70. Available from: <http://www.sciencedirect.com/science/article/pii/S0045653517315138>.
- Shakeri F, Roshan NM, Kaveh M, Eftekhari N, Boskabady MH. Curcumin affects tracheal responsiveness and lung pathology in asthmatic rats. *Pharmacol Reports [Internet]*. 2018; Available from: <http://www.sciencedirect.com/science/article/pii/S1734114018300021>.
- Punithavathi D, Venkatesan N, Babu M. Curcumin inhibition of bleomycin-induced pulmonary fibrosis in rats. *Br J Pharmacol*. 2000;131(2):169–72.
- Tian S, Xiong Y, Liu H, Niu L, Guo J, Liao M, et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. *Mod Pathol*. 2020;1–8.