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Review Article

A Comparative Review on Lung Detox from Smoking-Induced Lung damage

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Abstract:
Smoking induced Lung damage is the multifaceted pathological development, which is compelled by Oxidative stress, Chronic inflammation, epithelial dysfunction and structural remodelling. Although the lungs possess intrinsic self-repair mechanism which, includes mucociliary clearance, alveolar macrophage activations and DNA repair pathways, the degree of lung recovery still remains variable and mostly incomplete, even after smoking cessation. This review thoroughly examines the biological processes which reinforces the lung detox by emphasizing the role of intrinsic anti-oxidant system, pharmacological treatments, regenerative medicines and dietary interventions, in lung recovery. Recent researches indicates that, anti-oxidants such as glutathione, flavonoids, and curcumin can reduce oxidative stress, whereas Ayurvedic and herbal remedies such as *Vasaka* and *Tulsi* possesses mucolytic and anti-inflammatory properties. Nevertheless, the clinical translation of these interventions is still relatively underexplored. Furthermore, new stem cell therapies and pulmonary rehabilitation programs have shown promise in improving alveolar regeneration and functional recovery. Despite these advances, long-term epigenetic changes and irreversible structural changes in chronic smokers pose significant challenges. This paper provides a detailed, mechanistic analysis of lung detoxification, addressing current research gaps, translational barriers, and potential therapeutic directions. A multi-targeted approach that includes medical, nutritional, and lifestyle interventions appears to be the most effective strategy for optimising post-smoking lung recovery.

Keywords: *Lung Detoxification, Lung Regeneration, Smoking-induced damage, Chronic Obstructive Pulmonary Diseases, Intrinsic mechanism, Anti-oxidants, Ayurveda, Panchakarma*,

1. Introduction

Smoking is still most significant, yet preventable cause of respiratory disorders globally, responsible for Chronic Obstructive Pulmonary Diseases (COPD), Lung carcinoma and interstitial lung fibrosis. The cigarette smoke having the toxic composition of over 7,000 harmful chemicals, induces progressive oxidative stress, inflammatory cascades and structural lung damage [1]. These physiological changes not only affect the lungs but also the cardiovascular and immune system. Hence to cease smoking is the first and most critical step towards reducing the morbidity and mortality [2]. Although the extent to which the lungs can detox and heal itself post smoking remains uncertain, with various interventions proposed to speed up the recovery rate [3].

The phrase "Lung Detox" is frequently misinterpreted in mainstream conversations, alongside many commercial products falsely claiming to cleanse the lung tissues overnight. In actuality the lungs possess the intrinsic healing mechanisms, includes mucociliary clearance, alveolar macrophage-mediated phagocytosis, and endogenous antioxidant defences that help to detoxify the body gradually after smoking [4]. Although, the degree of prior damage restricts the mechanisms, particularly in the cases of emphysema and lung fibrosis at which the tissue loss in highly irreversible [5]. The idea that lung can regenerate completely after years after cessation of smoking is not scientifically accepted, so it makes is critical to distinguish the natural recovery process from unsupported detox claims [3].

Following the smoking cessation, lungs undergoes through a complex recovery process involving cellular repair, oxidative stress reduction inflammation modulation [6]. Mucociliary function tends to improve within the weeks of quitting smoking, along with cilia regrowth restoring mucus clearance efficiency. Alveolar macrophages removes the residual toxins and necrotic cellular debris, but their function is compromised in long term smokers due to chronic oxidative stress cilia regrowth restoring mucus clearance efficiency [7].

At the molecular level, Nrf2-regulated anti-oxidative pathways neutralizes the Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) originated from cigarette smoke, thus enhancing lung detox [8]. Although the chronic smokers suffer from dysregulated Nrf2-signalling, resulting into prolonged oxidative damaged and impaired DNA repair mechanisms [9]. Matrix Metalloproteinases (MMPs) and Transforming Growth Factor-Beta (TGF- β) signalling causes structural damage to alveoli, leading to irreversible emphysematous changes and limited lung regeneration [5].

Comprehending the scientific reality of the lung detoxification becomes essential to develop evidence-based interventions can substantially promote lung recovery in ex-smokers. Even though some intrinsic self-repair mechanisms are effective, certain lung injuries, particularly those caused by alveolar destruction and fibrosis, are permanent and necessitate novel therapeutic approaches [10]. This review extensively investigates the lung damage mechanisms the extent to which natural detox process can restore smoke induced damage as well as the role of dietary, herbal, medicinal as regenerative interventions to promote lung recovery. The focused topics of this review includes, the pathophysiology of smoking-induced lung damage, including cellular and molecular damage mechanisms; natural detoxification mechanisms, including immune response, mucociliary clearance, and endogenous antioxidants; dietary and pharmaceutical interventions, such as antioxidants, anti-inflammatory compounds, and pharmacotherapy; herbal and ayurvedic approaches, such as phytochemicals and traditional medicine in lung healing; modern medical approaches, such as stem cell therapy, pulmonary rehabilitation, and advanced lung treatments; and comparative analysis of lung detox strategies, which includes evaluating various interventions and their limitations as well as looking into new therapeutic targets and translational medicine approaches.

2. PATHOPHYSIOLOGICAL ASPECTS OF SMOKING-INDUCED LUNG DAMAGE

The pathophysiological effects of smoking include oxidative stress, chronic inflammation, mitochondrial dysfunction, alveolar remodelling, and DNA damage in the lungs, all of which are responsible for the COPD, Lung Cancer and Pulmonary fibrosis [1]. Cigarette smoke consists of toxic chemicals specifically reactive oxygen species (ROS), reactive nitrogen species (RNS), and carcinogenic substances, which may trigger a Cascade of cellular and molecular events that degrade lung function. Understanding these pathways is crucial for exploring potential detoxifying and therapeutic approaches to reducing smoking-induced lung harm. Cigarette smoke produces a significant amount of ROS and RNS, which overwhelms the body's endogenous anti-oxidant defence system, which leads to lipid peroxidation, protein oxidation, and DNA damage [4]. ROS, particularly superoxide anions (O_2^-), hydroxyl radicals (OH•), and peroxynitrite ($ONOO^-$), directly damages the lung cells triggering apoptosis and necrosis. The enzyme NADPH oxidase (NOX), plays a key role in amplifying oxidative stress, especially by promoting the activation of NOX2 in macrophages, which maintains chronic inflammation in smokers [8].

Smokers have significantly compromised anti-oxidant response, generally mediates via Nuclear factor erythroid 2-related factor 2 (Nrf2). Nrf2 generally controls expression of anti-oxidant enzymes which includes superoxide dismutase (SOD), catalase (CAT) and glutathione (GPx) [9]. Although the prolonged cigarette exposure results in epigenetic knockout of Nrf2 target genes, hence limiting the lungs ability to counteract the oxidative damage [11]. The consequence is the chronic oxidative stress, persisting even after quitting smoking, causing long term lung dysfunction. Smoking triggers a pro-inflammatory condition, characterized by high cytokinin levels, immune cell infiltration and recurring lung tissue damage. Major inflammatory mediators are, Tumour Necrosis Factor (TNF-α), which activates the macrophages and forces alveolar destruction; Interleukin-6 (IL-6) and Interleukin-1β (IL-1β) promotes fibroblast and proliferation and airway remodelling and Interleukin-8 (IL-8) facilitates neutrophilic inflammation promoting excess mucus secretion [12].

Macrophages, the first line of defence, changes phenotypically in accordance to chronic smoking. Under normal circumstances M1 macrophages act as pro-inflammatory scavengers, eradicating pathogens and apoptotic cells. Although smoking triggers a shift towards M2 macrophage polarization, promoting fibrosis and airway remodelling [5]. This imbalance results in chronic inflammation and slows healing of lung damages. Neutrophil activation also serves as a key factor in Lung damage. Neutrophils release Neutrophil Elastase (NE) and Matrix Metalloproteinases (MMPs), when exposed to smoke, damages elastin and collagen in alveolar walls, contributing to emphysematous destruction [10]. Failure to maintain the proteolytic activity causes irreversible damage resulting to COPD. Destruction of alveolar structures is one of the most irreversible consequences of smoking, leading to progressive emphysema. This is primarily driven by excessive protease activity (high MMP-9 & MMP-12 levels); elastin degradation, causing loss of lung elasticity and perpetual alveolar apoptosis and capillary loss, limiting gas exchange efficiency [7].

Fibrotic remodelling is another aspect of smoking-related lung pathology. Chronic smokers possess elevated levels of Transforming growth factor-beta (TGF-β), a fibrogenic cytokine which activates fibroblasts, increases collagen deposition and stiffens lung tissues [9]. This subsequently leads to progressive airway obstruction and dropped lung compliance, which indicates chronic bronchitis and pulmonary fibrosis. Furthermore, cigarette smoke disrupts airway epithelial homeostasis, resulting in squamous metaplasia and goblet cell hyperplasia. These structural changes are linked to increased mucus production, decreased mucociliary clearance, and chronic airway obstruction [13].

Smoking induced-lung damage goes beyond just hurting cells, leading to permanent genetic and epigenetic alterations which affect disease progression. Important epigenetic alterations include, DNA methylation, where smoking increases the methylation of tumour suppressor genes (p53, RASSF1A, CDKN2A), raising lung cancer risk [6]; Histone acetylation and methylation of histones alter chromatin structure, impacting antioxidant & DNA repair genes and MicroRNA (miRNA) dysregulation, certain miRNAs, such as miR-146a and miR-155, are upregulated in smokers, promoting inflammation and tissue destruction [14]. Cigarette smoke contains carcinogenic compounds like benzo[a]pyrene, nitrosamines, and formaldehyde, which induce DNA adducts and cause mutations in oncogenes (KRAS) and tumour supressing genes (TP53) [1]. These mutations play a significant role in the development of lung cancer, which explains why ex-smokers continue to be at a higher risk of malignancy decades after quitting.

Lung detox proves challenging due to the intricate interactions between Oxidative stress, chronic inflammation, proteases-antiprotease imbalance and epigenetic changes. Chronic smokers experience irreversible emphysematous as well as fibrotic damage, whereas mucociliary clearance is improved after smoking cessation. Anti-oxidants can supress oxidative stress but cannot reverse mitochondrial dysfunction or DNA mutations. Stem cell-based therapies are being explored, yet their clinical applications are being restricted due to ethical and technical challenges. With these complexions an effective detox strategy must address multiple pathways along with inflammation resolution, antioxidant support, and potential regenerative therapies.

3. INTRINSIC LUNG DETOX MECHANISM

The lungs possess intrinsic detoxification mechanisms which allows the expulsion of inhaled toxins and promote cellular repair after smoking cessation. These processes encompass mucociliary clearance, alveolar macrophage-mediated endogenous anti-oxidant defences and limited tissues generation. Although these processes gradually improve lung function post smoking cessation, yet their efficacy depends on severity of prior damage, especially in cases of COPD and pulmonary fibrosis.

Mucociliary clearance is the primary mechanism of lung detox, clearing inhaled pollutants, microbial pathogens and excess mucus. This is a mechanism, wherein the movement of mucus along the airway epithelium driven by cilia helps in the expulsion of trapped particulates. It is well established that chronic smoking disrupts this system as toxic effects of formaldehyde, acetaldehyde and hydrogen cyanide paralyze the ciliary motion and promote goblet cell hyperplasia that causes excess mucus production and airway obstruction [7]; known to downregulate surfactant proteins (SP-A & SP-D), important in lung immune defence & pathogen clearance [9].

After smoking cessation, cilia regenerate within several weeks and restores mucus clearance function. Although in Chronic smokers, having prolonged epithelial damage, mucociliary function stays partially impaired, resulting to chronic cough and sputum retention [5]. Alveolar macrophages, lungs primary immune cells serve a key role in removal of necrotic cells, inhaled particles and microbial invaders. In smokers, macrophages exhibit diminished phagocytic activity, limiting the clearance of apoptotic cells and toxic substances [8]. Chronic immune dysregulation is led by prolonged activation of inflammatory pathways [12]. Elevated iron levels results into oxidative stress and alveolar destruction. Alveolar macrophages restore functionality after smoking cessation, but full recovery may take months or years, according to severity of prior damage [11].

RNS and ROS generated by smoke is neutralized by lungs' endogenous anti-oxidants. The Nrf2 Pathway and Glutathione & Xenobiotic Metabolism are primary defence mechanisms. Nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor responsible for activating expression of Anti-oxidant response elements (AREs). The major anti-oxidant enzymes regulated by Nrf2 involves Superoxide dismutase (SOD), Glutathione peroxidase (GPx) and Heme oxygenase-1 (HO-1), which converts superoxide radicals into less toxic hydrogen peroxide, facilitates the conversion of hydrogen peroxide to water, reducing oxidative damage and plays a protective role in oxidative stress-induced lung injury respectively [8]. Although, prolonged smoking result in supressing Nrf2 due to epigenetic changes, thus impairing lungs' ability to neutralize oxidative stress [9]. Post smoking cessation, Nrf2 activity gradually renews, but in chronic smokers, persistent oxidative stress might inhibit lung detox efficiency [1].

Glutathione (GSH), a major lung anti-oxidant, hinders ROS-induced lipid peroxidation and assist in detoxification by directly neutralizing ROS, peroxides and free radicals. Glutathione-S-transferase (GST) catalyses conjugation reactions, promoting removal of toxic metabolites. NADPH dependant pathways aids in regeneration by retaining redox balance [15]. Glutathione depletion, experienced by smoker, impairs lung detoxification. Post-smoking cessation, GSH levels gradually return to normal, aiding lungs to detox residual toxins [10].

Cigarette smoke induces CYP1A1 and CYP2E1, cytochrome (CYP) P450 enzymes, in lungs which metabolizes xenobiotics and endogenous compounds, causing bioactivation of carcinogens like benzo[a]pyrene [1]. Post smoking cessation, Phase I enzymes (CYP450 family) slowly downregulate, thus limiting the formation of toxic intermediates and Phase II enzymes i.e. Glucuronosyltransferases (UGTs) and sulfotransferases (SULTs) promotes the conjugation and elimination of toxins. Although in chronic smokers having severe DNA damage, thses pathways might prove ineffective, increasing the possibility of long-term lung cancer [3].

Although the endogenous detox mechanisms support lung healing, yet are inadequate for complete lung generation, specifically in individuals with chronic bronchitis and mucus hypersecretion, which impairs mucociliary clearance. Excess collagen deposition results into fibrotic remodelling, reducing tissue elasticity and limiting oxygen exchange [5].

The MMPs degrade elastin and cause intense, irreversible destruction of the alveoli and emphysematous changes [7]. Divergent small cellular subtypes: These unique populations are capable of DNA damage repair and associated with negating these smoke-induced epigenetic modifications that simultaneously inhibits lung detox and limits cellular capacity [6]. Such dysregulated histone acetylation leads to perpetuated inflammatory gene expression [14]. In view of these limitations, those endogenous detoxification mechanisms alone are insufficient; and external strategies, including nutritional, pharmacogenic, and regenerative therapy, are required to enhance the restoration of the lungs [2].

4. NUTRITIONAL AND ANTI-OXIDANT THERAPIES IN LUNG REPAIR

Post smoking Lung detox depends on anti-oxidant mechanisms which neutralizes oxidative stress, reinstate immune balance and promote cellular repair. Dietary and pharmacological anti-oxidants are responsible to combat the RNS and ROS, which are heavily generated in smokers, contributing to alveolar damage, DNA mutation and chronic inflammation [4]. Although, lungs have intrinsic anti-oxidant mechanism such as glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT), which tends to disrupt in chronic smokers thus necessitating the additional interventions to boost lung detox and tissue recovery [8]. Nutritional interventions provide a promising, non-invasive strategy to reduce oxidative stress, promote lung function recovery, and mitigate inflammation. Additional dietary anti-oxidants. Various dietary anti-oxidants, notably vitamin C & E, polyphenols, flavonoids, omega-3 fatty acids, exhibited potential in lung detox [9]. Nevertheless, few clinical researches signify positive effect, the overall bioavailability, metabolism and prolonged efficiency of these compounds are still being explored [11].

Dietary anti-oxidants neutralize free radicals, reduce inflammation and enhance pulmonary function. Smoking degrades major anti-oxidants, leading to prolonged oxidative damage to the lung tissues, these must be replenished by diet and supplementation [12]. Vitamin-C (Ascorbic Acid) is potential water-soluble anti-oxidant which directly neutralizes ROS, specifically hydroxyl radicals and superoxide anions, thus preventing lipid peroxidation and DNA damage. It also supports collagen synthesis, which is necessary for tissue repair and preserving alveolar integrity [10]. Ex-smokers with greater vitamin-C intake have lesser airway inflammation and enhanced pulmonary functions compared to those with deficiencies [15]. Vitamin-E (Tocopherol), a fat-soluble anti-oxidant, prevents oxidative damage to the cell membranes by neutralizing lipid peroxyl radicals. Its supplementation has been proven to enhance lung elasticity and supress airway hyper-responsiveness in ex-smokers. Although, the long-term impacts of vitamin-E in avoiding COPD progression remains uncertain, as hyper supplementation might disrupt immune homeostasis [1].

Polyphenols and flavonoids, which are present in fruits, vegetables & tea, displays anti-inflammatory properties by modulation of Nrf2 pathway, which controls the expression of anti-oxidant response elements (AREs) in lung cells. Compounds such as quercetin (present in onions & apples), resveratrol (grapes), and curcumin (turmeric) counter against oxidative lung injury. these compounds limit the lung tissue damage by supressing pro-inflammatory cytokines (TNF- α & IL-6), thus boosting endogenous anti-oxidant properties [7]. Omega-3 fatty acids, primarily found in fish oils, are crucial for reducing inflammation, as they regulate eicosanoid metabolism. Omega-3 supplementation limits airway inflammation improves oxygen exchange and slows down the declining lung function in ex-smokers [13]. Although their efficiency in reversing structural lung damage is limited, emphasizing the significance of combined therapeutic strategies [5].

However, dietary anti-oxidants aids in lung recovery, pharmacological compounds also offers target-specific intervention by stimulating endogenous detox pathways. N-Acetylcysteine (NAC) has been clinically proven as mucolytic agent and glutathione precursor, aiding in breakdown of excess mucus and neutralizing free radicals. NAC improves glutathione production, thus restoring lungs' primary anti-oxidant defence system [11]. Prolonged NAC intake enhances lung function, reduces COPD exacerbations and promotes toxin elimination in ex-smokers. Lycopene and Beta-Carotene are the carotenoid anti-oxidants, present in tomatoes and carrots have demonstrated to prevent oxidative damage to lungs' epithelial cells by neutralizing the singlet oxygen species ($^1O_2$). Clinical trials suggest, higher carotenoid intake is associated with a lowering the risk of COPD, yet supplementation alone cannot completely recover lung function [3]. Coenzyme Q10 (CoQ10) is a mitochondrial anti-oxidant, which aids in mitigating the oxidative stress in lung tissues while enhancing cellular energy metabolism. CoQ10 intake also demonstrated to enhance the pulmonary oxygen utilization while reducing fatigue in smokers [6]. However its long-term efficiency is still unproven.

Although anti-oxidant therapies have potential, their effectiveness in completely reversing smoking-induced damage is still undetermined. Several challenges like Bioavailability issues, lack of large-scale trials and potential pro-oxidant effect still exists. The therapeutic potential of many anti-oxidants is reduced by their absorption and fast metabolism, particularly in case of polyphenols and carotenoids [9]. Long term trials assessing the lung functions are still required accordingly as most of the studies prioritise short term benefits [10]. Sometimes high doses of some anti-oxidants, specifically, beta-carotene and vitamin-E may act as the pro-oxidants in smokers promoting the risk of cancer [1]. Due to these limitations, an integrated approach of pharmacological and lifestyle changes may be the best strategy to assist lung detox in ex-smokers.

5. *AYURVEDIC* AND *PANCHAKARMA* APPROACHES TO LUNG DETOX

Traditional medicinal practices, specifically *Ayurveda*, Traditional Chinese Medicines (TCM) and *Siddha*, have been long used as the herbal medicines for detoxification. Numerous plants have mucolytic, anti-inflammatory, bronchodilatory and anti-oxidant properties which makes them potential candidates to promote lung detox after smoking cessation [14]. Certain phytochemicals are found to modulate inflammatory pathways improve mucociliary clearance and promote lung detox via anti-oxidant mechanisms [16].

Tulsi (Holy basil, *Ocimum sanctum*) is an anti-inflammatory immune modulator shrub (also a herb), which contains eugenol, ursolic acid and rosemarinic acid, exhibiting anti-inflammatory and anti-oxidant effects [14] Tulsi extract helps to reduce oxidative stress in lung tissues, which makes it favorable to ex-smokers suffering from chronic inflammation. It regulates the cytokine expression, limiting TNF-α and IL-6 which are plays major role in lung inflammation. It promotes the mucociliary clearance, thus helping in eradicating smoke induced toxins [16]. *Vasaka* (Malabar nut, *Adusa*, *Justicia adhatoda*), a major bronchodilator and mucolytic shrub, is rich in bioactive alkaloids, like vasicine and vasicinone, having expectorant and bronchodilatory properties. It promotes bronchial smooth muscle relaxation which reduces airway compression. It enhances mucin secretion, aiding expulsion of excessive mucus in ex-smokers. Research demonstrates that *Vasaka* extracts boosts oxygen uptake and relieve breathing difficulties in ex-smokers. [17]. *Yastimadhu* (Licorice root, *Mulethi, Glycyrrhiza glabra*), frequently used in *Ayurveda* and *Siddha* medicines is an anti-oxidative & anti-fibrotic agent, which is rich in glycyrrhizin and liquiritigenin, aiding to inhibit NF-κB activation which is a major inflammatory pathway in COPD [18]. It avoids pulmonary fibrosis by regulating TGF-β signaling and collagen synthesis. It also boosts lungs anti-oxidant defences, which reduces alveolar damage induced by oxidative stress. *Haridra* (Turmeric, *Haldi, Curcuma longa*) contains curcumin, a powerful anti-oxidant and anti-inflammatory compound. It is a active compound which regulates Nrf2-dependent antioxidant pathways, thus limiting ROS-induced lung injury [19]. It limits lung fibrosis caused by long term smoking. It prevents the upregulated histone deacetylases (HDACs) which prevents long-term inflammatory gene expression. It inhibits benzo[a]pyrene-induced DNA adduct, thus can have potential anti-cancer effects. *Ardraka* (Ginger, *Adrak*, *Zingiber officinale*) ia a potential airway relaxant and detoxifier, containing gingerol and shogaol, which are natural bronchodilators [20]. It inhibits synthesis of leukotriene resulting into reduced airway inflammation. It also boosts glutathione (GSH) synthesis thus improving detoxification efficacy.

Traditional formulations such as *Dashamoola*, a blend of dried roots of ten distinct species, is used in *Ayurveda* medicine and *Pippali* (*Piper longum*) have been known for their mucolytic and anti-inflammatory properties, aids in clearing airways and reduction of oxidative stress. Certain *Panchakarma* therapies like *Nasya* and *Vamana* are believed to assist in eradicating respiratory toxins. Although their efficiency in smoking related disorders and lung damage is yet to be well researched [16]. In addition to it, the phytochemical studies on *Agasti* (*Sesbania grandiflora*) and *Vasaka* demonstrates that their bioactive compounds act as the anti-oxidants. Thus, aiding to neutralize the free radicals and supporting lung recovery. While previous research suggests the possible benefits yet scientific validation as well as clinical trials are desired to affirm their long-term effect and the optimum dosage for therapeutic use [21].

The use of herbal smoking alternatives is common in *Siddha* medicine. *Prayogika Dhumapana* is a technique of inhaling smoke medicinal properties. It is traditionally believed to clear the respiratory passages and irradicate toxins. However, there are concerns regarding the probable lung irritation, thus more research is necessary to validate its safety and efficiency in ex-smokers [21,22].

In spite of potential benefits of herbal medicines and *Ayurvedic* therapies, it is important to approach them with scientific scrutiny. Most of these *Ayurvedic* supplements do not have standard dosage and clinical validation, which makes its effect unpredictable. Furthermore, some *Ayurvedic* herbs may interact with medications, intensifying the need of medical supervision before employing them to lung detox plan. While herbal and *Ayurvedic* therapies produces promising lung detox solutions, they must be used along with modern medicinal treatments for the optimum results.

Panchakarma is a core *Ayurvedic* therapy for detoxification. Traditionally it is used to remove the toxins from the body and restore balance. It is comprised of five cleansing techniques, each one is aimed at distinct organ system, including respiratory system. Most of *Ayurvedic* experts believe that *Panchakarma* techniques helps to clear lung congestion, reduce inflammation and strengthens overall respiratory functions. *Vamana* (therapeutic emesis) is one of the most primary therapies used in *Panchakarma* for lung health. This technique includes the controlled induction of vomiting to expel excess mucus and toxins from the upper respiratory tract. It is traditionally used for cough related disorders, which includes chronic cough, bronchitis and excessive mucus production. Some studies have suggested that *Vamana* therapy improves the lung function in individuals with chronic respiratory disorders, but more clinical trials are needed to confirm its safety and efficiency. *Nasya* (nasal therapy) is another *Panchakarma* technique related to lung detox. In this therapy, medicated oil and herbal extracts are subjugated through the nostrils, aiming at the sinuses and respiratory tract. It is believed to clear nasal congestion, reduce respiratory tract inflammation and improve oxygen intake. Some studies demonstrates that *Nasya* therapy can intensify pulmonary functions and limit severity of smoking-related lung disorders, however its long-term effects remain vague. *Swedana* (a herbal steam therapy), another therapy in *Panchakarma* that is thought to aid lung detox by promoting sweating and clearing respiratory tract. It involves the use of medicinal herbal stem, when inhaled it loosens mucus buildup and improve lung ventilation. Steam inhalation with *Ayurvedic* herbs, such as *Tulsi* and *Vasaka* may help in removing accumulated toxins from respiratory tract. *Basti* (medicated enema therapy) is not directly related to lungs, but some *Ayurveda* texts assert that cleansing of colon can discursively aid in pulmonary health by balancing internal energy systems [13, 23].

Despite its ancient use these therapies remain highly anecdotal. Scientific validation of these therapies is a significant challenge. It lacks of standardization as variability in herbal formulations, extraction methods and active ingredient concentrations can affect therapeutic consistency [21]. Most of the studies are in-vitro or animal models, whereas limited randomized controlled trials (RCTs) on humans are being performed. Poor bioavailability and complex pharmacokinetics of phytochemicals may hinder their effectiveness in systemic circulation [16]. Possible herb-drug interaction in certain botanicals, such as liquorice and turmeric, can interact with anti-inflammatory drugs and corticosteroids, so use with caution [18].

6. MODERN MEDICAL INTERVENTIONS AND CURRENT RESEARCH IN LUNG DETOXIFICATION

Although intrinsic detox mechanism, Ayurvedic medicines, Panchakarma therapies and dietary changes offers particular benefits modern medicinal techniques still remains the mostly preferred scientifically proven method approach to enhance lung function upon smoking cessation. These interventions seeks to lower the inflammation, improve airway functioning, increase oxygenation and in particular instances regenerate lung tissue [9]. Pharmacological treatments, pulmonary rehabilitation, and advancing regenerative medicine techniques like stem cell therapy are being actively explored due to their abilities to reverse smoke-induced lung damage [6]. Pharmacotherapies or pharmacological treatments, proves effective in mitigating residual lung damage after smoking, specifically in individuals having chronic bronchitis, emphysema or impaired mucociliary clearance.

Bronchodilators are the primary medications that soothes the airway smooth muscles reducing bronchoconstriction and improve airflow. They are especially beneficial to the smokers having obstructive conditions such as COPD [12]. β2-Agonists, such as Salbutamol and Formoterol, stimulates β2-adrenergic receptors which results into improved airway dilation and oxygen exchange. Anticholinergics, such as Ipratropium and Tiotropium, blocks the muscarine receptors in airway smooth muscles, resulting in decreased airway constriction and mucus hypersecretion. Long-acting β2-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) are generally prescribed together due to their synergistic bronchodilation [13]. Bronchodilators, in actuality, do not repair lung damage, yet they significantly boost breathing capacity, specifically in case of ex-smokers with pervasive respiratory symptoms.

Individuals having post-smoking residual inflammation are benefitted from Inhaled Corticosteroids (ICS), reducing lung inflammation, preventing further airway remodelling [11]. Corticosteroids, such as Fluticasone and Budesonide reduces pro-inflammatory cytokines (IL-6 and TNF- α), alleviating airway inflammation. ICS and LABA are used in synergy specifically in individuals with persistent airway hyperreactivity. Oral corticosteroids such as Prednisone and Methylprednisolone, are intended only for severe acute exacerbations of chronic bronchitis. Prolonged use of corticosteroids must be avoided due to their potential side effects like immune suppression, osteoporosis and metabolic dysregulation [15].

Mucolytics are medications that thins out mucus by breaking down mucin glycoproteins or DNA and F-actin polymer networks, reducing airway obstruction and the risk of cystic fibrosis, bronchiectasis and COPD. N-Acetylcysteine (NAC) promotes glutathione synthesis which acts as both mucolytic and anti-oxidant, aiding in neutralizing ROS and facilitate mucus clearance. Erdosteine and Carbocisteine aids in reducing mucus viscosity and enhance airway hydration for better expectoration. Clinicals trails indicates that the long-term NAC therapy improves lung function and lowers exacerbations in individuals with chronic bronchitis [3].

Apart from these medicinal interventions, pulmonary rehabilitation and Oxygen therapy also found to aid in lung recovery. Pulmonary rehabilitation is a well-structured programme which improves individual's lung function by combined training exercises, breathing techniques and patient education [23]. Exercises enhances strength of respiratory muscles, thus improving ventilatory capacity and oxygen utilization. Breathing techniques like Pursed-Lip Breathing and Diaphragmatic Breathing aids to lower dyspnea and increasing lung expansion [20]. Diaphragm strength and respiratory endurance is improved by Inspiratory Muscle Training (IMT) aiding in oxygen delivery to tissues. According to clinical studies, ex-smokers with residual lung impairment benefit from routine pulmonary rehabilitation in terms of lung function, exercise tolerance, and quality of life [4].

Long-term Oxygen Therapy (LTOT) is prescribed to ex-smokers having severe emphysema or COPD to prevent chronic hypoxia. For individuals with advanced lung diseases High-Flow Oxygen Therapy is used to improve oxygen saturation and reducing work of breathing. Individuals experiencing exercise-induced oxygen desaturation, Intermittent Oxygen Supplementation can be beneficial. Although oxygen therapy only improves survival and exercise capacity, it cannot reverse the structural lung damage, which makes it just a supportive rather than curative intervention [5].

Recent advancements in regenerative medicines have prompted interest in Stem cell therapy for lung regeneration. Stem cells, specifically Mesenchymal Stem Cells (MSCs) have anti-inflammatory, immunomodulatory, and regenerative properties, thus rendering them a potential candidates for lung repair [6]. MSCs lowers the chronic inflammation in lung tissues by regulating the immune responses. They stimulate endogenous progenitor cells, promoting regeneration of alveolar epithelial tissue. They secrete paracrine factors to facilitate angiogenesis and tissue remodelling. Multiple early-phase clinical trials have assessed the potential of stem cell therapy for lung regeneration. In COPD patients, MSCs infusion have shown to reduce inflammatory markers, such as IL-6 & TNF-α, yet failed to significantly improve lung function [24]. Induced Pluripotent Stem Cells (iPSCs) for Alveolar Repair is still in its experimental stage although the preclinical models show promising results [9]. Despite its potential, stem cell therapy is faced by challenges like immune rejection, ethical concerns and potential carcinogenicity [13]. Hence, more research is required to demonstrate its clinical safety, efficiency and long-term benefits in lung detox [3].

7. PSYCHOLOGICAL, NEUROBIOLOGICAL AND BEHAVIOURAL ASPECTS OF LUNG DETOX

The lung detoxification post-smoking cessation is not only determined by biological and pharmacological rebounds, but also influenced by psychological resilience, behavioural adaptations and neurochemical reprogramming to it. Smoking addiction is not only a physical dependence on nicotine, but also includes habitual conditioning, emotional triggers and neural reward pathways [22]. Even though after smoking cessation most of the ex-smokers faces psychological withdrawal symptoms like stress, anxiety and depressive symptoms. These symptoms interfere lung recovery and support to relapse [3]. These psychological factors must be addressed when it comes to detoxification and optimal lung health.

Nicotine is the primary cause of smoking addiction. It stimulates the dopaminergic reward pathways in the brain specifically in the mesolimbic systems [12]. In ventral tegmental areas (VTAs) nicotinic acetylcholine receptors (nAChRs) are upregulated due to prolonged nicotine exposure, developing its dependence. Therefore, upon cessation, stress-induced relapses are led by dopaminergic spikes in the nucleus accumbens (NAcc), which results into cravings and withdrawal symptoms, and increased cortisol levels [4]. The withdrawal symptoms, such as irritability, anxiety, sleep disturbances, and cognitive impairment, faced by ex-smokers are driven by dopamine depletion and acetylcholine receptor desensitization [1].

Cognitive Behavioral Therapy (CBT) is one of the highly effective measures to terminate the habitual smoking, thus promoting lung detox. The main aim of the CBT is to determine and substitute the smoking stimuli, like stress & social triggers by using healthier coping mechanisms. It also focuses on cognitive restructuring in order to modify irrational convictions concerning smoking and detoxification. These Behavioural reinforcement therapies encompass selfmonitoring, positive reinforcement, and contingency management [22]. It is found out that ex-smokers undergoing CBT displays higher lung function improvement rates and decreased relapse rate, rather than those trying to quit without psychological assistance [7]. Mindfulness-Based Interventions (MBIs), which includes yoga, meditation and guided breathing have demonstrated to reduce smoke cravings, regulate stress responses and improve respiratory effectiveness. Ex-smokers can promote lungs expansion, improve oxygen exchange and regulate the autonomic nervous system function by engaging in controlled breathing therapies [23].

Smoking is often used as a instant stress-coping medium or for instant pleasure, quitting it suddenly may lead to increased anxiety and emotional dysregulation [11]. This psychological barrier hinders lung detoxification by elevation of cortisol levels, which mitigates chronic inflammation and reduce oxidative stress. It also decreases the compliance with the pulmonary rehabilitation programs due to motivation loss and limiting the breathing with decreased lung efficiency which is led by stress-induced respiratory dysregulation [4]. Although the behavioural treatments like guided relaxation, progressive muscle relaxation and cognitive framing have proven to improve psychological well-being and assist in lung function recovery in ex-smokers [3].

Social reinforcements and external support systems have a major role to prevent relapse, thus regulating the lung detox process. Individuals participating in group-based rehabilitation programs, family counselling or any online support network have greater compliance to quit smoking and lung detox mechanisms, with higher resilience to cravings and withdrawal-induced stress. They have stronger motivation for adopting pulmonary rehabilitation and exercise routines [2]. Anti-smoking campaigns such as WHO's "Commit to Quit", the CDC's "Tips From Former Smokers" American Lung Association's "Freedom From Smoking Program", "1-800-QUIT-NOW" counselling services, and Indian government's "*Nasha Mukt Bharat Abhiyan*" (Toll-free helpline: 14446) provide well-structured psychological and behavioural support, aiding ex-smokers to maintain motivation and prolonged lung health.

8. COMPARATIVE ANALYSIS OF VARIOUS LUNG DETOX APPROACHES

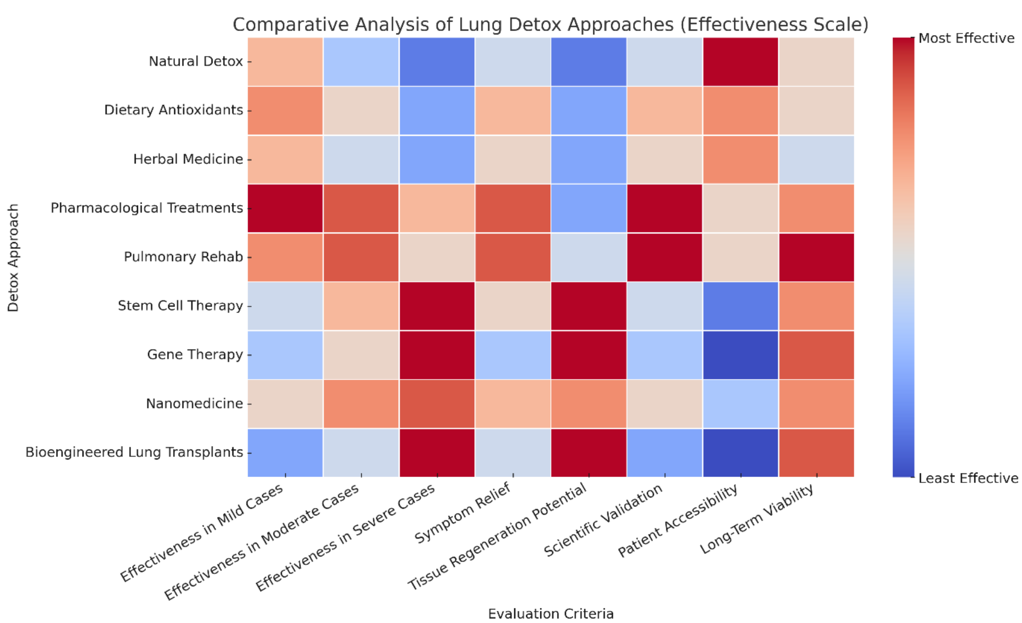

Figure 1: Heatmap for Comparative Analysis of Various Lung Detox Approaches

This heatmap of Comparative Analysis Lung detox approaches were designed by creating a local dataset with integration of clinical trial data, meta-analyses, and expert reviews altogether. These scores were assigned by evaluating overall aspects of each approach. We assigned scores to each approach on the basis of factors like scientific validation, effectiveness in different lung conditions, and patient-centred factors. This scoring system and evaluation method was guided by the studies conducted by Giordano et al. (2015), Cantin (2010), Hecht (1994, 1996), and the American Lung Association (2024). The scores in case of Effectiveness in Mild, Moderate and Severe Cases were from evaluating their usefulness in evaluating lung function recovery, inflammation reduction, and symptom relief. Scientific Validation scores for the approaches were based on evaluation of the RCTs, FDA approvals, and systematic reviews. And at last, the factors like symptom relief, accessibility, and long-term viability were patient-centred and scores were assigned by using outcomes and adherence rates as mentioned in various studies. This scoring system was again re-evaluated and compared against Large Language model i.e. DeepSeek, known as the best LLM to analyze textual data and scientific insights, whose outcomes were almost same with the considerable variation, thus validated our scoring system.

Pulmonary rehabilitation and pharmacological treatments scored highest in the category of sustained benefits while stem cell therapy and gene therapy (discussed in next section) were better at regeneration but not available for everybody. Natural detox and antioxidants were also among the methods that were easily achieved however they barely affected the cases. By these scores the balance between scientific rigor and practical application is properly kept.

As mentioned earlier most of lung detox approaches shows promise but not all lung damage is reversible. The recovery rate depends upon if, structural or functional impairments dominate the condition. In case of Reversible damage, Mucociliary function can reinstate in few weeks to months after cessation, macrophage activity gradually improves, inflammatory cytokines slowly lower while reducing lung tissue irritation and anti-oxidant enzyme systems (Nrf2, glutathione, SOD) can repair & improve oxidative-stress control. While in case of irreversible changes, degradation of elastin and matrix remodelling in emphysema leads to a permanent loss of alveolar elasticity. Destruction of lung parenchyma leads to fibrotic changes including irreversible airway stiffening that outlasts any specific intervention. Lung cancer risk is enhanced by DNA mutations and epigenetic changes, and persists even decades after smoking cessation. So, while some degree of lung detoxification is possible, they declared, a full reversal of smoking damage to the lungs is biologically impossible.

A personalized lung detox approach is necessary for the individuals by taking in account their severity in lung damage. For individuals with mild damage, like cough, mucus accumulation and airflow blockage intrinsic detox mechanisms, dietary anti-oxidants pulmonary rehab and herbal approach might be adequate. Over the time mucociliary clearance and immune function recovers. Combination therapy involving bronchodilators, mucolytics (NAC) and dietary anti-oxidants may be sufficed for the individuals with moderate damage, such as chronic bronchitis, reversible airway obstruction, persistent cough. In case of Individuals with severe damage like Emphysema, Fibrosis, COPD and Lung Cancer Risk pharmacological interventions (ICS + LABA, Long-term Oxygen therapy) is must

9. FUTURE SCOPE AND RESEARCH DIRECTIONS

Lung detoxification and recovery post-smoking cessation is a hot topic in current research fields, with new interventions to regulate, repair and restore lung function, tissue damage and reduce chronic inflammation. Existing interventions offers symptomatic relief but are unable to reverse the structural and epigenetic lung damage. Henceforth, novel therapeutic interventions like stem cell therapy, gene editing, epigenetic reprogramming and nanomedicines are under investigation to revitalize lung integrity at cellular and molecular levels.

Stem cell-based regenerative therapy is one of the most promising therapies in lung detox, seeking to repair damaged alveolar damage and reinstate pulmonary function. In current times, Mesenchymal Stem Cells (MSCs) and Induced Pluripotent Stem Cells (iPSCs) for lung regeneration are the main focus of research. Bone marrow, adipose tissue, or umbilical cord blood derived MSCs have exhibited to possess anti-inflammatory, immunomodulatory, and tissue-regenerative properties. iPSCs offer personalised lung regeneration to patients, preventing the risks like immune rejection associated with allogenic stem cell transplants. However, Stem cell therapy faces challenges like transplanted may have low survival and engraftment rates in impaired lung tissues. The alveolar regeneration is hindered by fibrotic micro environment, also the uncontrolled cellular proliferation may increase the risk of tumorigenesis. However, clinical trials are still looking into the safety and efficiency of stem cell therapy, particularly in COPD, pulmonary fibrosis and post-cessation lung repair, the large-scale validation is still needed.

Gene therapy and epigenetic reprogramming is another promising and novel technique for lung repair. Although it is still in its emerging state. Smoking contributes to perpetual epigenetic changes, which involves DNA methylation, histone modifications, microRNA dysregulation which alters gene expression, leading to lung inflammation, fibrosis and carcinogenesis. [11]. CRISPR-Cas9 is a gene editing technique, which is still being investigated to repair the smoke-induced mutations in Tumour supressing genes, such as TP53 & RASSF1A, thus reducing risk of lung cancer [5]. Histone deacetylase (HDAC) inhibitors and DNA demethylating agents, like 5-azacytidine are under investigation to reverse fibrosis related gene fibrosis [8]. MicroRNA (miRNA)-based treatments seeks in mitigating inflammatory and oxidative stress pathways, specifically focussing miR-155 and miR-146a, that are associated with chronic lung diseases [12]. This therapy is still in its preclinical stages due to safety concerns, off-target effects, and ethical considerations [3].

Recently, Nanotechnology-based drug delivery systems for Targeted Lung Detoxification are being studied for improving anti-oxidant therapies, drug bioavailability and molecular targeting of inflammation [10]. Current innovations focus on inhalable nanoparticles, which encapsulates anti-inflammatory agents like curcumin, quercetin, and omega-3s along with nanoparticle-based antioxidant carriers for targeted delivery of NAC, glutathione, and resveratrol to alveolar cells to improve lung bioavailability [20]. The CRISPR-loaded lipid nanoparticles (LNPs) are under investigation to correct gene expression in emphysematous lung [23] Nanomedicine possesses the potential to overcome the shortcomings in conventional drug delivery system, although certain issues like toxicity, biocompatibility, and scalability require more research [9].

Bioengineered lung transplants and extracorporeal lung support systems care being investigated as a future treatment option for individuals with severe irreversible damage. [7]. 3D Bioprinting of Functional Lung Tissue is also an emerging technology concerning the issue. Researchers are focused on creating bio-printed alveolar structures from patient derived cells to create functional lung graft transplantation [18]. Extracorporeal Carbon Dioxide Removal (ECCO_2R) may serve as promising interventions for patients with severe COPD and hypercapnic respiratory failures. It aids to offload CO_2 whilst preserving lung function [15]. Artificial Alveoli Technology focuses on synthesizing synthetic alveolar units imitate the gas exchange could eventually be more preferable instead of whole lung transplant [10]. While these technologies are still in the experimental stage, they represent the future of personalized lung detoxification and transplantation therapy.

In spite of the advances in research, several research gaps still exist. Most novel therapies i.e. stem cells, gene therapy still remain in pre-clinical stages and require human validation due to lack of large-scale clinical trials. The efficiency of long-term anti-oxidant, such as NAC, polyphenols, vitamin C & omega-3 fatty acids, still needs proper investigation. Research must be focused on if the smoking-induced epigenetic changes can be reversed with interventions like epigenetic dregs or lifestyle changes [1]. By integrating AI in healthcare, machine learning models are being developed for prediction of lung function recovery, nevertheless they need to be refined further for real-life clinical applications [9].

10. CONCLUSION

Lung detox post-smoking cessation is a gradual process, having multiple aspects, involving various interventions like natural repair mechanisms, pharmacological support, lifestyle changes and novel regenerative therapies. Although mild to moderate lung damage can be alleviated through anti-oxidant therapy, pulmonary rehab and pharmacological treatments, yet severe structural damage at cellular level like alveolar destruction in emphysema is predominantly irreversible. Pharmacological interventions and rehabilitation strategies are most validated approaches for symptomatic relief and functional recovery, alongside natural and dietary intervention imparts additional support. Regenerative cell therapies live stem cell therapy and gene therapy offers great potential to reverse lung damage, yet being in experimental stages they require clinical validation.

Despite of all these advancements complete lung detoxification and regeneration is still a major scientific challenge emphasizing prevention being the most functional approach. Optimizing regenerative medicine, improving targeted drug delivery and integration of artificial intelligence into personalized lung detox plans must be the focus of future research. The future to lung detox lies in collaborating emerging medical innovations along with adopted rehabilitation protocols to develop patient-specific lung detox strategies to maximize lung recovery and long-term health. As prevention is always better than cure, we can conclude that Smoking cessation is still the most effective intervention as even the most advanced treatments are unable to completely reverse long-term smoking-induced damage.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no other interest to report.

AUTHORS' CONTRIBUTIONS

Authors AT, SV and SB[c] proposed the idea of the study and designed the structure of review. Authors SK and AN intervened and statistical analysis of the textual data using LLMs. TP, SB[f] and SG, in consultation with AT and SV wrote the paper with input from all authors. All authors provided critical feedback and helped shape the research, analysis and manuscript.

CONSENT

Not applicable

ETHICAL APPROVAL

The present research work does not contain any studies performed on animal/human subjects by any of the authors.

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