INDONESIAN JOURNAL OF MULTIDISCIPLINARY SCIENCE

P-ISSN: 2808-5957
E-ISSN: 2808-6724

Can Herbal Medicine Bridge the Gap in Smoking Cessation? A Review of Plant-Based Interventions for Nicotine Addiction (2021-2025)

Ebel Vigrajuska Asri*, Sarrah Ayu Hartanti
Universitas Riau, Indonesia
Email: ebel.vigrajuska0728@student.unri.ac.id*

ABSTRACT

Tobacco use remains a major global health challenge, with current cessation therapies limited by efficacy, accessibility, and side effects. This systematic review explores whether *herbal medicine* can provide effective, affordable plant-based interventions for nicotine addiction. We synthesized recent literature (2021–2025) from major open-access databases to evaluate phytotherapeutic agents targeting nicotine dependence and withdrawal. Our findings reveal several promising herbs with multifaceted pharmacological actions. *Piper nigrum* and *Acanthopanax koreanum* helped alleviate withdrawal symptoms and modulated neurological pathways linked to addiction. *Piper sarmentosum* and the combination of *Cinnamomum* (cinnamon) and *Zingiber officinale* (ginger) exerted protective effects against nicotine-induced oxidative stress. *Avena sativa* improved quality of life and reduced stress, indirectly supporting cessation. Notably, *Vernonia cinerea* significantly increased abstinence rates and reduced oxidative damage, with efficacy comparable to conventional pharmacotherapies. In contrast, evidence for *Hypericum perforatum* remains inconclusive, necessitating further research. This review highlights phytotherapy as a promising, accessible adjunctive approach to smoking cessation. To fully establish the therapeutic potential of these herbal interventions, future research should focus on standardized clinical trials, optimal dosing, and detailed investigation of underlying molecular mechanisms. Plant-based therapies may offer a valuable complement to existing cessation strategies, enhancing outcomes for individuals seeking to overcome nicotine addiction.

Keywords:
Smoking Cessation, Nicotine Addiction, Phytotherapy, Herbal Medicine, Medicinal Plants

INTRODUCTION

Tobacco use constitutes a major global public health crisis, with cigarette smoking remaining the leading preventable cause of chronic disease and death worldwide. The World Health Organization indicates that tobacco accounts for over 7 million deaths annually, including 1.6 million non-smokers exposed to secondhand smoke (WHO, 2025). Cigarette smoke contains thousands of

chemical compounds, many of which are highly toxic. These include tobacco-specific nitrosamines (TSNAs) such as N′-nitrosonornicotine (*NNN*) and *NNK*, potent carcinogens widely found in tobacco products (Hecht & Hatsukami, 2022). Consequently, smoking significantly elevates the risk of major non-communicable diseases (NCDs) such as lung and other cancers, chronic obstructive pulmonary disease (COPD), and cardiovascular and cerebrovascular diseases (Mitra et al., 2023). For instance, Bergman et al. (2022) observed that continued smoking during radiotherapy markedly increases tumor recurrence and reduces disease-free survival. In essence, tobacco smoke is a primary contributor to morbidity and mortality across multiple organ systems (Bergman et al., 2022).

Nicotine, the primary addictive component in tobacco, rapidly stimulates brain reward pathways by binding to nicotinic acetylcholine receptors, leading to dependence (Singh & Saadabadi, 2025). Beyond its addictive properties, nicotine promotes angiogenesis, cell proliferation, and survival in various tissues, potentially supporting tumor growth and spread in existing cancers (Sansone et al., 2023). Additionally, other chemicals in tobacco smoke, such as TSNAs like *NNN* and *NNK*, are strong carcinogens linked experimentally to cancers of the lung, esophagus, and other organs (Hecht & Hatsukami, 2022).

Over the past decades, governments and health agencies have implemented various tobacco control measures, including high cigarette taxes, advertising bans, mandatory pictorial health warnings, media campaigns, and smoke-free laws (Ismail et al., 2010; Maarof et al., 2016). Similarly, intensive behavioral efforts such as counseling and quitlines have been developed. These interventions can improve cessation: for example, WHO notes that combining counseling with pharmacotherapy more than doubles a smoker's chance of quitting. Graphic warning labels and hard-hitting media campaigns are also proven to reduce smoking initiation and encourage quitting (WHO, 2025). Despite these efforts, overall cessation rates remain suboptimal. Many smokers struggle to quit due to the powerful grip of addiction and social and psychological factors. Indeed, a substantial fraction of smokers continue to use tobacco even when fully aware of the health hazards. For example, recent surveys in the United States show that roughly 10% of high-school students currently use some form of tobacco (CDC, 2024), illustrating that young people may initiate or continue smoking despite knowledge of risks. In cancer care, continued smoking after diagnosis is known to worsen outcomes (Bergman et al., 2022). The study found that patients who smoked during radiotherapy had significantly higher recurrence rates and poorer survival than non-smokers. In short, relapse and sustained use remain common problems even with strong anti-tobacco measures (Bergman et al., 2022).

Several effective medications are available to aid smoking cessation, including nicotine replacement therapies (patches, gums, sprays, inhalers, lozenges) and non-nicotine drugs such as bupropion and varenicline (Singh &

Saadabadi, 2025). When properly used in conjunction with counseling, these treatments can significantly increase quit rates. However, achieving long-term abstinence remains challenging. Existing therapies often exhibit only moderate efficacy, leading to high relapse rates. They can also induce bothersome side effects, such as nausea, headache, or sleep disturbances (Mitra et al., 2023). Another significant barrier is cost and accessibility, particularly in low- and middle-income countries (LMICs), where essential cessation medications are often scarce or unaffordable (Plum et al., 2025). Thus, despite the existence of safe and effective conventional medicines, their global accessibility and tolerability remain limitations.

Given these challenges, there is a pressing need for novel cessation aids that are both effective and affordable. Natural products, specifically plant extracts and *herbal* remedies with long traditional use, represent a promising avenue. Globally, the use of traditional and complementary medicine is substantial, with lifetime or annual prevalence ranging from 20% to 70% across various countries (Lee et al., 2022), indicating broad cultural acceptance and availability. While rigorous data on *phytotherapeutic* treatments specifically for nicotine addiction are still emerging, research interest is growing. A 2023 meta-analysis, for instance, reported that certain herbal preparations (*Vernonia cinerea*, *Hypericum perforatum* [St. John's wort], lavender oil) were associated with significantly higher continuous abstinence rates among smokers compared to controls (Mitra et al., 2023). Black pepper (*Piper nigrum*) and other botanicals have also shown some benefit in reducing cigarette cravings. These preliminary findings suggest that botanicals may hold potential for aiding smoking cessation, potentially with fewer side effects and lower costs than conventional drugs (Mitra et al., 2023).

This review systematically surveys recent scientific literature (2021–2025) on plant-derived compounds for treating nicotine addiction. We systematically collected open-access studies of herbs and natural products tested for smoking cessation or nicotine dependence. Our objective is to summarize candidate *herbal* agents, their active constituents, and the available evidence regarding their efficacy and mechanisms of action. By doing so, this review aims to highlight the most promising *phytotherapeutic* treatments that could be developed as future pharmacological aids to smoking cessation, either alone or in combination with standard therapies.

RESEARCH METHODS

This research employed a systematic literature review and publication search across several open-access databases, including Google Scholar, PubMed, ScienceDirect, SpringerLink, Scopus, and ResearchGate. Data sources were selected according to inclusion criteria covering studies published between 2021 and 2025, written in English or Indonesian, available in full text, and consisting of research or review articles focusing on plants with herbal content affecting human or animal subjects in both observational

and experimental designs. The search specifically targeted potential *herbal* plants for reducing nicotine addiction. Search phrases combined terms such as *"herbal medicine"* OR *"medicinal plants"* OR *"herbal treatment"* OR *"herbal supplement"* OR *"traditional medicine"* AND *"smoking cessation"* OR *"nicotine addiction"* OR *"tobacco dependence"* OR *"smoking withdrawal"* OR *"quit smoking."*

Following retrieval, duplicates were removed, and two independent researchers screened titles, abstracts, and full texts for relevance. Extracted data from selected studies included study design, plant species, active phytochemicals, administration methods, and key outcomes related to smoking cessation efficacy. The findings were synthesized into a coherent narrative emphasizing pharmacological mechanisms and clinical potential of each *herbal* plant.

This approach aligns with prior systematic reviews that demonstrated *herbal* medicines such as *Vernonia cinerea*, *Hypericum perforatum* (St. John's wort), lavender essential oil, black pepper (*Piper nigrum*), and others can significantly increase continuous and point abstinence rates and reduce cravings without major adverse effects, supporting their promise as adjuncts or alternatives to conventional tobacco cessation therapies.

RESULTS AND DISCUSSION

Table 1. Summary of Herbal Plants with Potential in Reducing Nicotine Addiction (2021-2025)

Author(s)	Plant	Type of Study	Key Compounds	Activity and Potential
Weleff et al. (2022)	Black Pepper (*Piper nigrum*)	Case report (burnt pepper inhalation); Review of two small clinical trials (EO vaporization)	Black pepper essential oil; Burnt Pepper Powder	Reduced nicotine withdrawal symptoms and craving through sensorimotor and anxiolytic effects; supports further research on vaporized EO for smoking cessation.
Md. Salleh MFRR et al. (2021)	Piperaceae (*Piper sarmentosum)*	In vivo (rat model); Experimental design	Flavonoids, alkaloids, phenolic compounds in AEPS[and]	AEPS enhanced vasorelaxation by increasing nitric oxide (NO) and antioxidant activity (SOD, CAT, GSH)[b], reducing ROS[c]. Improved nicotine-induced endothelial dysfunction by increasing NO bioavailability and reducing oxidative stress.
Friling et al. (2024)	Wild Green Oat (*Avena sativa L.)*	Double-blind placebo RCT (8 weeks; NCT04749017)	Neuravena® green oat extract (900 mg/day)	Improved QoL[g] (WHOQOL-BREF, SF-36), reduced stress & improved sleep quality during smoking reduction/cessation; safe & well-tolerated.

Author(s)	Plant	Type of Study	Key Compounds	Activity and Potential
Lee et al. (2024)	*Acanthopanax korenum* (AK)	Rat behavioral study (CPP, sensitization, SA); dopamine ELISA; Western blot	70% ethanol extract; Eleutheroside B & Chlorogenic acid	Suppressed nicotine dependence & withdrawal symptoms in rats: normalized dopamine, nAChR α7 expression, DRD1-EPAC-ERK-CREB; promising natural agent for smoking cessation.
Walia et al. (2021)	St. John's Wort (*Hypericum perforatum*)	Systematic review of RCT SJW (4 studies)	SJW extract (300–600 mg TID)	Abstinence & craving: minimal changes vs placebo; well-tolerated; evidence inconclusive, larger RCTs needed.
Kanthain R et al. (2024)	*Vernonia cinerea*	Clinical Trial (adolescent smokers); Breathing exercise + *V. cinerea* hard candy	Nicotine (2.35 mg/candy), Total phenolics (3.76 mg/candy), Total flavonoids (0.42 mg/candy)	Increased 7-day PARs[d] (90%) and CAR[e] (80%) after 8 weeks. Decreased MDA[f] and increased GSH[b]. Effective in reducing oxidative stress.
De Santi O et al. (2024)	*Vernonia cinerea*	Systematic Review & Meta-Analysis (RCTs)	Flavonoids (apigenin, chrysocriol, luteolin, quercetin); hirsutinolide-type sesquiterpene lactones	Inhibited CYP2A6 and MAO; increased nicotine and dopamine bioavailability; effective for smoking cessation (<15 cigarettes/day); good safety profile.
Tuenthosarn et al. (2023)	*Vernonia cinerea*	Open-label RCT vs nortriptyline (12 weeks + follow-up)	VC extract (apigenin, luteolin, quercetin, hirsutinolid, nitrate)	CAR similar to nortriptyline; ↓ cigarettes/day; different AE profile (bitter tongue vs dry mouth, drowsiness); Effective and safe.
Luetragoon et al. (2021)	*Moringa oleifera Lam.* (MO) & *Cyanthillium cinereum* (Less.) H. Rob. (CC)	Double-blinded RCT on volunteer smokers	Astragalin, phenolic compounds, antioxidants (DPPH activity)	Reduced gingival index (GI) and oral inflammation; potential for oral health. Suppressed bacterial plaque and reduced smoking craving; holistic strategy for oral health and smoking cessation support.
Taha et al. (2021)	Cinnamon & Ginger	Experimental study on adult male albino rats	Cinnamon oil, Ginger oil	Combination of cinnamon and ginger oils significantly reduced oxidative stress and degenerative changes caused

Author(s)	Plant	Type of Study	Key Compounds	Activity and Potential
				by nicotine in the prefrontal cortex.

Notes:
[a]AEPS: Aqueous extract of *Piper sarmentosum*
[b]SOD: Superoxide dismutase, CAT: Catalase, GSH: Reduced glutathione
[c]ROS: Reactive oxygen species
[d]PARs: Point prevalence abstinence rates
[e]CAR: Continuous abstinence rate
[f]MDA: Malondialdehyde
[g]QoL: Quality of Life

Black Pepper (*Piper nigrum*)

Black pepper (*Piper nigrum*) has long been recognized for its active compounds, such as piperine, which possess various pharmacological effects, including antioxidant, anti-inflammatory, and neuroprotective properties (Takooree *et al.,* 2019). However, its clinical utilization in the context of nicotine addiction therapy remains very limited and rarely reported.

A relevant case report by Weleff et al. (2022) described a unique phenomenon where a former inmate used burnt black pepper as a self-medication attempt to manage nicotine withdrawal symptoms. The patient reported that inhaling smoke from black pepper alleviated withdrawal symptoms such as anxiety, irritability, and impulsive cravings for smoking.

Three main mechanisms are suspected to play a role: first, the reduction of automatic urges, which are proven to be the strongest type of craving and directly related to abstinence failure (Wehbe *et al.,* 2018). Second, the anxiolytic effects of piperine, as demonstrated in preclinical studies showing sedative and antidepressant activity through the reduction of oxidative stress in the brain (Hritcu *et al.,* 2015; Wattanathorn *et al.,* 2008). Third, the fulfillment of sensorimotor experiences resembling tobacco smoking, including chest sensations, a bitter-spicy taste, and repetitive hand-to-mouth movements (Rose & Behm, 1994; Palmer *et al.,* 2021).

Interestingly, the practice of burning black pepper as a tobacco substitute was not only carried out individually but was reportedly widespread among other inmates in the correctional facility where the patient was held. This indicates a form of "collective knowledge" within prison culture regarding alternative ways to cope with substance addiction, which unfortunately has not been extensively explored in scientific literature (Richmond *et al.,* 2009). This experience emphasizes the importance of considering informal or unconventional approaches that organically develop in marginalized communities as considerations for alternative therapy development.

While burning black pepper is certainly not suitable for widespread therapy due to potential health risks from the resulting smoke, this finding reinforces the urgency to further investigate the use of vaporized black pepper

essential oil as a safer intervention. Previous studies have shown that black pepper essential oil aromatherapy can significantly reduce nicotine craving, even surpassing other essential oils like angelica (Cordell & Buckle, 2013). Therefore, further studies examining the effectiveness, optimal dosage, and safety of black pepper essential oil in smoking cessation are highly recommended.

Piperaceae (*Piper sarmentosum*)

In addition to *Piper nigrum*, the plant *Piper sarmentosum Roxb.* also shows pharmacological potential in the context of nicotine exposure, particularly in preventing nicotine-induced vascular endothelial dysfunction. Nicotine in cigarette smoke has significant cardiotoxic effects, including impairing vascular relaxation and reducing nitric oxide (NO) levels, a crucial molecule in maintaining vascular tone.

An experimental study by Salleh et al. (2021) demonstrated that the administration of an aqueous extract of *Piper sarmentosum* leaves (AEPS) significantly improved endothelium-mediated vascular relaxation, increased vascular NO levels, and enhanced antioxidant activities such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) in nicotine-induced rats. The decline in vascular relaxation due to nicotine is caused by oxidative stress, which increases the production of reactive oxygen species (ROS), thereby inhibiting eNOS (endothelial nitric oxide synthase) activity and reducing NO availability (Salleh *et al.,* 2021). AEPS was proven to restore this relaxation response, both in endothelialized and de-endothelialized blood vessels, indicating broad vasoprotective activity. The study also showed that AEPS maintained the normal histological structure of the aorta disrupted by chronic nicotine exposure, although no significant morphometric differences were found.

In an experimental study by Md. Salleh et al. (2021) the administration of an aqueous extract of *Piper sarmentosum* leaves (AEPS) significantly improved endothelium-mediated vascular relaxation, increased vascular NO levels, and enhanced antioxidant activities such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) in nicotine-induced rats. The decline in vascular relaxation function due to nicotine is caused by oxidative stress, which increases the production of reactive oxygen species (ROS), thereby inhibiting eNOS (endothelial nitric oxide synthase) activity and reducing NO availability (Md. Salleh *et al.,* 2021). AEPS was proven to restore this relaxation response, both in endothelialized and de-endothelialized blood vessels, indicating broad vasoprotective activity. The study also showed that AEPS was able to maintain the normal histological structure of the aorta disrupted by chronic nicotine exposure, although no significant morphometric differences were found.

The main proposed mechanism involves stimulating NO synthesis through increased eNOS activity, as well as protecting NO from degradation

by ROS through the direct antioxidant effects of flavonoid compounds in AEPS, such as quercetin, naringenin, and vitexin. These findings are important in the context of developing plant-based supportive therapies for individuals with chronic nicotine exposure, including passive smokers. Unlike *Piper nigrum*, which primarily affects craving and the sensorimotor aspects of smoking behavior (Weleff *et al.,* 2022), *Piper sarmentosum* works systemically through vascular biochemical and antioxidant pathways. This suggests that phytotherapy approaches can be directed not only to aid smoking cessation but also to reduce the physiological damage already caused by nicotine.

Green oat extract (GOE) of *Avena sativa L.*

Oatmeal sativa L., particularly in the form of wild green oat extract marketed as Neuravena, has shown significant potential in supporting the process of smoking reduction or cessation. The mechanism of action of this supplement is assumed to be rooted in its activity as a monoamine oxidase-B (MAO-B) inhibitor, which increases dopamine availability in the brain. This is crucial in the context of nicotine cessation, as low dopamine activity often causes withdrawal symptoms such as depression, anhedonia, and fatigue (Friling *et al.,* 2024).

In an eight-week randomized, double-blind, placebo-controlled study involving 161 adult active smokers, the group receiving 900 mg/day of *Avena sativa* extract showed significant improvements in quality of life (QoL), physical and psychological health aspects, and stress and sleep parameters compared to the placebo group. A significant decrease in stress scores measured by the Perceived Stress Scale (PSS), an increase in vitality and mental health domains based on SF-36, and improved sleep quality (especially a reduction in wakefulness after sleep onset – WASO) indicate that Neuravena not only reduces the psychological burden of smoking cessation but also supports overall well-being recovery (Friling *et al.,* 2024).

Interestingly, although no significant differences were found between the intervention and placebo groups in terms of nicotine dependence, withdrawal symptoms, or craving after cue exposure, the proportion of participants who successfully reduced daily cigarette consumption by ≥20% was significantly higher in the Neuravena group (66.7%) compared to placebo (49.3%). This suggests that the subjective improvement in psychophysical well-being encouraged participants to be more successful in reducing cigarette consumption (Friling *et al.,* 2024).

Thus, *Avena sativa* can be viewed as a plant with a phytotherapeutic approach that does not directly target nicotinic receptors pharmacologically like nicotine replacement therapy, but rather intervenes in the psychological and physiological aspects that exacerbate the smoking cessation experience. By improving sleep quality, reducing stress, and increasing vitality, *Avena*

sativa-based intervention offers a holistic approach highly relevant to tobacco reduction or cessation efforts.

***Acanthopanax korenum* (AK)**

Acanthopanax koreanum Nakai, a member of the Araliaceae family endemic to Jeju Island, South Korea, has long been used as a tonic and sedative in traditional medicine. In the context of modern pharmacology, the stem extract of this plant, particularly in the form of a 70% ethanol extract, shows significant potential in reducing nicotine addiction symptoms and withdrawal syndrome.

A recent experimental study by Lee et al. (2024) comprehensively demonstrated that *A. koreanum* extract and its two main active components, eleutheroside B (EB) and chlorogenic acid (CGA), were able to reduce the rewarding effects of nicotine through a series of behavioral tests in rats, including conditioned place preference (CPP), locomotor sensitization, and self-administration. In the CPP test, nicotine-induced rats showed a significant increase in place preference, reflecting the rewarding effects of the substance. However, administration of *A. koreanum* extract (100–200 mg/kg), EB, or CGA significantly decreased CPP scores, indicating reduced motivation for nicotine exposure (Lee *et al.,* 2024). This effect was reinforced by the results of the locomotor sensitization test, where repeated nicotine administration led to increased motor activity as an expression of dopaminergic sensitization; this phenomenon was significantly suppressed by AK extract administration, especially at a dose of 200 mg/kg. Furthermore, withdrawal parameters such as tremors, rearing, and shaking also showed a global score reduction in the groups receiving AK extract, EB, and CGA, compared to the nicotine-control group.

The molecular mechanisms underlying this effect involve the normalization of the expression of several important proteins in the dopaminergic and nicotinic pathways, such as nAChR α7 in the ventral tegmental area (VTA), as well as a decrease in dopamine levels in the nucleus accumbens (NAcc), which usually increase sharply due to nicotine exposure. Furthermore, AK extract also reduced the expression of DRD1 (dopamine receptor D1), as well as the activation of EPAC2–ERK–CREB, a signaling pathway known to be closely associated with synaptic plasticity and addictive behaviors (Carlezon *et al.,* 2005; Lee *et al.,* 2024). This effect appeared more prominent with the whole AK extract than with single administrations of EB or CGA, indicating the potential synergism of phytocomponents in producing broader neuropharmacological effects.

These findings reinforce the relevance of *A. koreanum* as a candidate for alternative phytotherapy to support nicotine addiction therapy. Unlike conventional approaches that often target nAChR α4β2 receptors or use nicotine replacement therapy (NRT), *A. koreanum* demonstrates multidimensional effects: reducing craving, preventing dopaminergic

sensitization, alleviating withdrawal symptoms, and normalizing the expression of addictive proteins. Thus, this plant has the potential not only as a supplement for smoking cessation therapy but also as a long-term neuroprotective agent against the damaging effects of nicotine consumption.

St. John's Wort (*Hypericum perforatum*)

The results of this systematic review indicate that the use of St. John's Wort (SJW) as an intervention for smoking cessation has not shown significant effectiveness compared to placebo. Four randomised controlled trials (RCTs) that met the inclusion criteria reported a mean reduction in cigarettes smoked and craving symptoms over a 12–14 week period, but there was no statistically significant difference between the intervention and placebo groups (Camfield *et al.,* 2015; Sood *et al.,* 2010; Parsons *et al.* 2009; Lawvere *et al.,* 2006). For example, in the Sood *et al.* (2010) study, although nicotine withdrawal symptoms and craving decreased over time, abstinence rates at weeks 12 and 24 did not differ between the SJW (300 mg or 600 mg) and placebo groups. These findings are consistent with the Parsons et al. (2009) study, which reported an odds ratio (OR) for prolonged abstinence of 0.49 (95% CI: 0.13–2.93) at six months, indicating the ineffectiveness of SJW as both monotherapy and in combination with chromium.

Nevertheless, the safety profile of SJW in this context is noteworthy. All studies reported good tolerability to SJW, with mild side effects such as headache, nausea, and fatigue occurring sporadically (Lawvere *et al.,* 2006). This aligns with previous evidence demonstrating the safety of SJW in the treatment of depressive disorders (Fava *et al.,* 2005; Sarris *et al.,* 2012). However, the neurobiological mechanisms of SJW, which are suspected to affect serotonin and dopamine pathways, also involved in nicotine addiction were not sufficiently strong to produce a significant therapeutic effect in the context of smoking cessation. This indicates that despite pathophysiological similarities between depression and addiction, SJW-based interventions may require a multimodal approach combining behavioral therapy or other pharmacological agents to enhance effectiveness (Taylor *et al.,* 2017).

Major limitations in the existing studies include small sample sizes (n=20–145) and a high risk of bias in two out of four studies, particularly regarding outcome measurement and data reporting. Furthermore, the heterogeneity of intervention designs, such as the combination of SJW with nicotine replacement therapy (NRT) or chromium makes generalization of findings difficult (Camfield *et al.,* 2015; Parsons *et al.,* 2009). Meta-analysis could not be performed due to variations in statistical parameters and a high risk of bias, thus precluding definitive conclusions. On the other hand, the lack of psychosocial intervention in study designs may be a hindering factor, given that successful smoking cessation often requires holistic support (Lindson *et al.,* 2019). In the future, high-quality RCTs with larger samples and longer follow-up periods are needed to evaluate the potential of SJW more accurately.

Integration with evidence-based interventions such as cognitive-behavioral therapy (CBT) or intensive counseling is also worth testing to observe synergistic effects (Boyce *et al.,* 2018). Additionally, exploration of population subgroups, such as smokers with comorbid depression, might provide new insights given SJW's effectiveness in mood disorders (Sarris *et al.,* 2012).

***Vernonia cinerea* (VC)**

The combination of non-pharmacological interventions and *Vernonia cinerea* (VC) extract supplementation shows significant potential in supporting smoking cessation efforts. A study by Kanthain et al. (2024) evaluated the effects of relaxed deep-breathing with chest mobilization (rDB/CME) and hard candy containing VC extract in adolescent active smokers. The results showed that the group receiving the rDB/CME and VC combination had significantly increased 7-day point prevalence abstinence rates (90% at week 8) and continuous abstinence rate (80%) compared to the placebo or control groups. This mechanism is suspected to be related to increased glutathione (GSH) levels and decreased malondialdehyde (MDA), indicators of oxidative stress, suggesting an antioxidant role of VC in reducing cell damage from smoking. These findings are consistent with previous research reporting that flavonoids and nicotine in VC inhibit CYP2A6 and monoamine oxidase (MAO) enzymes, which are involved in nicotine and dopamine metabolism, thereby reducing dependence (Kanthain *et al.,* 2022; Prasopthum *et al.,* 2015).

A recent study by Tuenthosarn et al. (2023) compared the efficacy of VC with nortriptyline, a non-nicotine replacement therapy (non-NRT) drug. The results of an open-label randomized clinical trial showed no significant difference in continuous abstinence rate (CAR) between the two groups after 24 weeks (41.67% vs 43.24%). However, the side effect profiles differed: VC caused a bitter taste or numbness in the tongue (61.9%), while nortriptyline more frequently triggered dry mouth (90.48%) and drowsiness (90.48%) (Tuenthosarn *et al.,* 2023). This confirms VC as a safer alternative for patients with contraindications to anticholinergic effects or those requiring high physical activity.

Despite its promise, limitations such as small sample sizes, short intervention durations, and variations in VC extraction methods need to be addressed in future research. Dose optimization, product formulation (such as candies, teas, or pastilles), and more in-depth molecular mechanism studies are needed to validate VC as an effective and affordable adjuvant therapy for smoking cessation, especially in developing countries with high smoking prevalence.

***Moringa oleifera Lam.* (MO) & *Cyanthillium cinereum* (Less.) H. Rob. (CC)**

Moringa oleifera (MO) and *Cyanthillium cinereum* (CC) were evaluated as active ingredients in anti-inflammatory lozenges for smokers. Research by Luetragoon *et al.* (2021) showed that the combined MO+CC lozenges significantly reduced the gingival index (GI) (*$p<0.05$), while single MO lozenges provided the highest reduction in oral inflammation (81.48%)*. This activity is associated with MO's high phenolic content (245.14 mg GAE/g) and antioxidant capacity (330.79 μM TE/100 mg), as well as the presence of astragalin as a chemical marker. MO inhibits the NF-κB pathway by downregulating TNF-α, IL-6, and IL-8 expression, while CC increases anti-inflammatory IL-10. A double-blind randomized clinical trial on 67 smokers confirmed the safety and efficacy of these lozenges without hepatorenal side effects. The combination of both extracts not only suppressed bacterial plaque but also reduced smoking craving, making it a holistic strategy for oral health and supportive smoking cessation therapy (Luetragoon *et al.,* 2021). The reduction in craving might be attributed to a combination of improved oral health, potentially leading to a more positive sensory experience in the mouth, and the overall physiological benefits of reduced inflammation and oxidative stress, indirectly influencing psychological well-being associated with cessation.

Cinnamon & Ginger

Research by Taha et al. (2021) investigated the antioxidant effects of ginger oil, cinnamon oil, and their combination on morphological changes in the prefrontal cortex induced by nicotine. The aim of this study was to understand how compounds in ginger and cinnamon can protect the brain from the harmful effects of nicotine. This research employed an experimental design using adult male albino rats divided into five groups: a control group, a nicotine-only group, a nicotine and cinnamon oil group, a nicotine and ginger oil group, and a group treated with nicotine and a combination of cinnamon and ginger oils. The researchers measured oxidative stress markers (MDA, GSH) and observed morphological changes in the rats' prefrontal cortex. The results showed that the combination of cinnamon and ginger oils significantly reduced oxidative stress and degenerative changes caused by nicotine in the prefrontal cortex compared to the nicotine-only group. The conclusion of this study was that ginger and cinnamon are potent antioxidants with the potential to mitigate the neurotoxic effects of nicotine in rats.

Although this study demonstrated positive effects, it is important to note that the research was conducted on animals and focused on neurotoxicity, not directly on addiction reduction or smoking cessation. The question of whether these neuroprotective effects can translate into a reduction in addictive behavior or withdrawal symptoms in humans requires further investigation. Furthermore, the synergistic effect of the combination of cinnamon and ginger oils suggests that the interaction between bioactive compounds in these two

plants may produce a more potent therapeutic effect, which warrants further exploration.

CONCLUSION

The phytotherapeutic approach to smoking cessation shows promising potential through multiple mechanisms, including neurological modulation, psychophysiological support, and protection against nicotine-induced organ damage. Plant extracts such as *Piper nigrum* effectively mitigate withdrawal symptoms and cravings, while *Piper sarmentosum* provides vascular protection by reducing oxidative stress. *Avena sativa* enhances quality of life by alleviating stress and improving sleep, indirectly aiding smoking reduction, and *Acanthopanax koreanum* offers neuroprotective effects by normalizing dopaminergic pathways implicated in dependence. However, evidence for *Hypericum perforatum* remains inconclusive. Future research should prioritize larger, standardized clinical trials, optimize dosages and formulations, and further elucidate the molecular mechanisms underlying these effects to establish phytotherapy as a safe, effective, and affordable adjunctive treatment for smoking cessation, especially in regions with high smoking prevalence.

REFERENCES

Bergman, M., Fountoukidis, G., Smith, D., Ahlgren, J., Lambe, M., & Valachis, A. (2022). Effect of smoking on treatment efficacy and toxicity in patients with cancer: A systematic review and meta-analysis. *Cancers*, *14*(17), 4117. https://doi.org/10.3390/cancers14174117

Boyce, J. H., Chepkin, S. C., Ye, W., Bullen, C., & Lancaster, T. (2018). Nicotine replacement therapy versus control for smoking cessation. *Cochrane Database of Systematic Reviews*, *2018*(5), CD000146.

Camfield, D. A., Scholey, A. B., Pipingas, A., Stough, C., Schloeffel, R., Kelly, B., & Pase, M. P. (2015). The neurocognitive effects of *Hypericum perforatum* Special Extract (Ze 117) during smoking cessation. *Phytotherapy Research*, *27*(11), 1605-1613. https://doi.org/10.1002/ptr.4909

Carlezon, W. A., Duman, R. S., & Nestler, E. J. (2005). The many faces of CREB. *Trends in Neurosciences*, *28*(8), 436-445. https://doi.org/10.1016/J.TINS.2005.06.005

Centers for Disease Control and Prevention. (2024). *Smoking and tobacco use: Youth and tobacco use*. https://www.cdc.gov/tobacco/php/data-statistics/youth-data-tobacco/index.html

Cordell, B., & Buckle, J. (2013). The effects of aromatherapy on nicotine craving on a U.S. campus: A small comparison study. *The Journal of Alternative and Complementary Medicine*, *19*(8), 709-713.

De Santi, O., Di Niro, C. A., Rungruanghiranya, S., & Greco, V. (2024). Evaluation of the effectiveness of *Vernonia cinerea* for the treatment of

smoking cessation: A systematic review and meta-analysis. *Research Square*. https://doi.org/10.21203/rs.3.rs-5263865/v1

Fava, M., Alpert, J., Nierenberg, A. A., Mischoulon, D., Tedlow, J. R., Alpert, J. E., Ogden, L. G., Rosenbaum, J. F., & Yeung, A. (2005). A double-blind, randomized trial of St John's wort, fluoxetine, and placebo in major depressive disorder. *Journal of Clinical Psychopharmacology*, *25*(5), 441-447.

Friling, M., García-Muñoz, A. M., Lavie, A., Pérez-Piñero, S., Victoria-Montesinos, D., López-Román, F. J., García-Guillén, A. I., Muñoz-Carrillo, J. C., Cánovas, F., Ivanir, E., & Jalanka, J. (2024). Dietary supplementation with a wild green oat extract (*Avena sativa* L.) to improve wellness and wellbeing during smoking reduction or cessation: A randomized double-blind controlled study. *Frontiers in Nutrition*, *11*, Article 1405156. https://doi.org/10.3389/fnut.2024.1405156

Hecht, S. S., & Hatsukami, D. K. (2022). Smokeless tobacco and cigarette smoking: Chemical mechanisms and cancer prevention. *Nature Reviews Cancer*, *22*(3), 143-155. https://doi.org/10.1038/s41568-021-00423-4

Hritcu, L., Noumedem, J. A., Cioanca, O., Hancianu, M., Postu, P., & Mihasan, M. (2015). Anxiolytic and antidepressant profile of the methanolic extract of *Piper nigrum* fruits in beta-amyloid (1-42) rat model of Alzheimer's disease. *Behavioral and Brain Functions*, *11*(1), 13.

Ismail, R., Syed Aljunid, S. M. A., Latip, K. A., & Puteh, S. E. W. (2010). Effectiveness of group counseling in smoking cessation program amongst adolescent smokers in Malaysia. *Medical Journal of Indonesia*, *19*(4), 273-279.

Kanthain, R., Leelarungrayub, J., Likhitsathian, S., & Natakankitkul, S. (2024). Efficacy of combined relaxed deep-breathing with chest mobilization exercise and *Vernonia cinerea*-hard candy on smoking cessation and oxidative stress in active teenage smokers. *Pharmacognosy Journal*, *14*(6), 720-727. https://doi.org/10.5530/pj.2022.14.159

Lawvere, S., Mahoney, M. C., Cummings, K. M., Kepner, J. L., Hyland, A., Lawrence, D. D., Lando, H., & Fiore, M. C. (2006). A phase II study of St. John's wort for smoking cessation. *Complementary Therapies in Medicine*, *14*(3), 175-184. https://doi.org/10.1016/j.ctim.2006.01.007

Lee, E. L., Richards, N., Harrison, J., & Barnes, J. (2022). Prevalence of use of traditional, complementary and alternative medicine by the general population: A systematic review of national studies published from 2010 to 2019. *Drug Safety*, *45*(7), 713-735. https://doi.org/10.1007/s40264-022-01189-w

Lee, H. J., Ortiz, D. M., Sayson, L. V., Kim, M., Cheong, J. H., & Kim, H. J. (2024). Ameliorating effects of *Acanthopanax koreanum* extract and components on nicotine dependence and withdrawal symptoms. *Addiction Biology*, *29*, e13360. https://doi.org/10.1111/adb.13360

Lindson, N., Klemperer, E., Hong, B., Ordóñez-Mena, J. M., & Aveyard, P. (2019). Smoking reduction interventions for smoking cessation. *Cochrane Database of Systematic Reviews*, *2019*(9), CD013183. https://doi.org/10.1002/14651858.CD013183.pub2

Luetragoon, T., Sranujit, R. P., Noysang, C., Thongsri, Y., Potup, P., Somboonjun, J., Maichandi, N., Suphrom, N., Sangouam, S., & Usuwanthim, K. (2021). Evaluation of anti-inflammatory effect of *Moringa oleifera* Lam. and *Cyanthillium cinereum* (Less) H. Rob. lozenges in volunteer smokers. *Plants*, *10*(7), 1336. https://doi.org/10.3390/plants10071336

Maarof, M. F., Ali, A. M., Amit, N., Bakry, M. M., & Taha, N. A. (2016). Suitability of a group behavioural therapy module for workplace smoking cessation programs in Malaysia: A pilot study. *Asian Pacific Journal of Cancer Prevention*, *17*(1), 207-214.

Md. Salleh, M. F. R. R., Aminuddin, A., Hamid, A. A., Salamt, N., Japar Sidik, F. Z., & Ugusman, A. (2021). *Piper sarmentosum* Roxb. attenuates vascular endothelial dysfunction in nicotine-induced rats. *Frontiers in Pharmacology*, *12*, Article 667102. https://doi.org/10.3389/fphar.2021.667102

Mitra, R., Rai, A., Kumar, A., & Mitra, J. K. (2023). Role of herbal medication in tobacco cessation treatment: A systematic review and meta-analysis. *Addiction & Health*, *15*(1), 63-70. https://doi.org/10.34172/ahj.2023.1290

Palmer, A. M., Sawyer, L. E., & Brandon, T. H. (2021). Distinct influences of nicotine and sensorimotor stimuli on reducing cravings to smoke and vape among dual users. *Addictive Behaviors*, *122*, 107051.

Parsons, A., Ingram, J., Inglis, J., Aveyard, P., Johnstone, E., Brown, K., & Bisset, K. (2009). A proof of concept randomised placebo controlled factorial trial to examine the efficacy of St John's wort for smoking cessation and chromium to prevent weight gain on smoking cessation. *Drug and Alcohol Dependence*, *102*(1-3), 116-122. https://doi.org/10.1016/j.drugalcdep.2009.02.006

Plum, C., Stolbrink, M., Ozoh, O., Jayasooriya, S., Nightingale, R., Mortimer, K., & Halpin, D. (2025). Availability, cost and affordability of essential medicines for smoking cessation in low-income and middle-income countries: A cross-sectional study. *Thorax*, *80*(4), 248-250. https://doi.org/10.1136/thorax-2024-222391

Prasopthum, A., Pouyfung, P., Sarapusit, S., Srisook, E., & Rongnoparut, P. (2015). Inhibition effects of *Vernonia cinerea* active compounds against cytochrome P450 2A6 and human monoamine oxidases, possible targets for reduction of tobacco dependence. *Drug Metabolism and Pharmacokinetics*, *30*(2), 174-181. https://doi.org/10.1016/j.dmpk.2014.12.005

Richmond, R., Butler, T., Wilhelm, K., Wodak, A., Cunningham, M., & Anderson, I. (2009). Tobacco in prisons: A focus group study. *Tobacco Control*, *18*(3), 176-182.

Rose, J. E., & Behm, F. M. (1994). Inhalation of vapor from black pepper extract reduces smoking withdrawal symptoms. *Drug and Alcohol Dependence*, *34*(3), 225-229. https://doi.org/10.1016/0376-8716(94)90160-0

Sansone, L., Milani, F., Fabrizi, R., Belli, M., Cristina, M., Zagà, V., de Iure, A., Cicconi, L., Bonassi, S., & Russo, P. (2023). Nicotine: From discovery to biological effects. *International Journal of Molecular Sciences*, *24*(19), 14570. https://doi.org/10.3390/ijms241914570

Sarris, J., Fava, M., Schweitzer, I., & Mischoulon, D. (2012). St. John's wort (*Hypericum perforatum*) versus sertraline and placebo in major depressive disorder: Continuation data from a 26-week RCT. *Pharmacopsychiatry*, *45*(7), 275-278. https://doi.org/10.1055/s-0032-1306348

Singh, D., & Saadabadi, A. (2025). Varenicline. In *StatPearls*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK534846/

Sood, A., Ebbert, J. O., Prasad, K., Croghan, I. T., Bauer, B., & Schroeder, D. R. (2010). A randomized clinical trial of St. John's wort for smoking cessation. *Journal of Alternative and Complementary Medicine*, *16*(7), 761-767. https://doi.org/10.1089/acm.2009.0445

Taha, M., Ibrahim, M. M., Eldesoqui, M., Iesa, M. A. M., Baokbah, T. A. S., & Sonpol, H. M. A. (2021). Ameliorating effect of combined cinnamon and ginger oils against the neurotoxicity of nicotine administration on the prefrontal cortex of adult albino rats: Immunohistochemical and ultrastructural study. *Pharmaceutical Sciences*, *89*(4), Article 41.

Takooree, H., Aumeeruddy, M. Z., Rengasamy, K. R. R., Zengin, G., Khan, J., & Mahomoodally, M. F. (2019). A systematic review on black pepper (*Piper nigrum* L.): From folk uses to pharmacological applications. *Critical Reviews in Food Science and Nutrition*, *59*(Supplement 1), S210-S243.

Taylor, G., Aveyard, P., Meer, R. V., Toze, D., Stuijfzand, B., Kessler, D., & Munafò, M. (2017). Impact of variation in functions and delivery on the effectiveness of behavioural and mood management interventions for smoking cessation in people with depression: Protocol for a systematic review and meta-analysis. *BMJ Open*, *7*(12), e018617. https://doi.org/10.1136/bmjopen-2017-018617

Tuenthosarn, K., Budkaew, J., Sorncha, N., & Chumworathayi, B. (2023). Efficacy and safety of *Vernonia cinerea* for smoking cessation: An open-label randomized controlled trial. *Asian Pacific Journal of Cancer Prevention*, *24*(1), 101-106. https://doi.org/10.31557/APJCP.2023.24.1.101

Walia, N., Gonzalez, S., & Zoorob, R. (2021). A systematic review of the use of St. John's wort for smoking cessation in adults. *Cureus*, *13*(10), e18769. https://doi.org/10.7759/cureus.18769

Wattanathorn, J., Chonpathompikunlert, P., Muchimapura, S., Priprem, A., & Tankamnerdthai, O. (2008). Piperine, the potential functional food for mood and cognitive disorders. *Food and Chemical Toxicology*, *46*(9), 3106-3110.

Wehbe, L., Ubhi, H. K., & West, R. (2018). Want, need and habit as drivers of smoking behaviour: A preliminary analysis. *Addictive Behaviors*, *76*, 135-138.

Weleff, J., Dore, S., Anand, A., & Barnett, B. S. (2022). Black pepper (*Piper nigrum*) for tobacco withdrawal: A case report. *Case Reports in Psychiatry*, *2022*, Article 5908769. https://doi.org/10.1155/2022/5908769

World Health Organization. (2025). *Tobacco: WHO fact sheet*. https://www.who.int/news-room/fact-sheets/detail/tobacco