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A NARRATIVE REVIEW OF PUERARIA LOBATA'S EFFICACY IN LUNG CANCER MANAGEMENT

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Abstract
Lung cancer, a significant cause of cancer-related deaths globally, primarily attributed to smoking, remains a major public health concern. This article delves into the potential of Pueraria lobata, commonly known as kudzu, in managing lung cancer. Beginning with an overview of lung cancer prevalence, types, and treatment challenges, the article transitions into discussing kudzu's traditional medicinal uses, emphasizing its historical significance in Chinese medicine. Notably, puerarin, a key compound in kudzu, has exhibited anticancer properties in various studies, including inhibition of cell proliferation and induction of apoptosis. The article further explores the pharmacological properties of kudzu, its chemical composition, and mechanisms of action relevant to lung cancer treatment, elucidating its potential as a chemotherapeutic agent. Preclinical studies, both in vitro and in vivo, demonstrate promising results in inhibiting tumor growth and inducing cell death. Clinical evidence, although limited, suggests the efficacy of kudzu-based treatments in managing lung cancer, with some cases showcasing improvement in symptoms and disease progression. However, safety considerations and adverse effects must be carefully evaluated, especially in individuals with specific medical conditions or those taking certain medications. Overall, the aim of this article is to review the existing literature on Pueraria lobata's efficacy in lung cancer management, shedding light on its potential as a complementary or alternative therapeutic approach in combating this deadly disease.

Keywords: Lung Neoplasms, Pueraria, Antineoplastic Agents, Phytoestrogens, Traditional Medicine, Chemotherapy, Adjuvant

I. Introduction

A. Background on lung cancer prevalence and treatment challenges

Moreover referred to as bronchogenic carcinoma, lung cancer is the term for tumors that originate either from inside the bronchi or the lung tissue. It is among the main reasons why people die from cancer. Lung cancer is most frequently caused by smoking. Ninety percent of lung cancer cases are thought to be related to smoking. The majority of afflicted men are smokers. Exposure to extra carcinogenic substances, such as asbestos, increases the risk considerably [1].

The two main types of lung cancer are small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). There are more subcategories within the latter group. The WHO's 2015 classification names neuroendocrine cancers, including squamous cell carcinoma (SCC), adenocarcinoma (tumors of glandular cells), large cell neuroendocrine cancer (LCNEC), and carcinoid as the most prevalent kinds of lung cancer [2]. The most current GLOBOCAN data indicates that 2,094,000 new cases with lung cancer were recorded worldwide in 2018, making it the most frequent kind of cancer overall. With over Lung cancer became the second most frequent cancer in men, after prostate cancer, with 1,369,000 occurrences. It is the second most common cancer in women, behind breast cancer, with approximately 725,000 cases. Lung cancer is included into the 2020 Global Disease Statistics report maintained its position as the primary cause of cancer-related mortality globally, resulting in around 1.8 million deaths [2,3].

Drawing upon information according to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, the US has around 229,000 newly diagnosed cases of lung cancer in 2020, which represented 12.7% of all cancer diagnoses. Although several Western countries have observed a comparable pattern, developing nations like China and the former Soviet Union have not achieved similar progress in terms of smoking cessation and the occurrence of lung cancer. Currently, in China, 65% of males begin smoking by their mid-20s, indicating that there will be a sustained rise in the occurrence of lung cancer for many years to come [3,4].

Surgical excision of the tumor, together with adjuvant therapy, is the recommended treatment for stage I or II NSCLC. Conversely, as the disease progresses to stage III or IV, the treatment approach transitions to chemotherapy or radiotherapy. Nevertheless, nearly all conventional chemotherapeutic medications share common drawbacks, such as indiscriminate targeting, limited absorption, and the emergence of drug resistance, which ultimately restricts their effectiveness in treating cancer [5,6].

B. Overview of Pueraria lobata (Kudzu) and its traditional medicinal uses

Kudzu is classified within the Fabaceae family, specifically the Papilionoideae subfamily, Phaseoleae tribe, Glycininae subtribe, and Pueraria genus. Van der Maesen described a total of 17 species that are officially recognized and classified under the name Pueraria. Kudzu is a perennial vine that climbs and has semi-woody stems covered in hairy rusty-brown fibers. Puerariae Lobatae Radix, derived from the root of P. lobata (Willd.) Ohwi is a medicinal herb that has been used in ancient China from early times. It is alternatively referred to as Gegen, Yegen, or Kudzuvine root [6,7]. The therapeutic properties of kudzu root were initially recorded in the Divine Husbandman's Classic of Chinese Materia Medica during the Western Han Dynasty (206 BC–8 AD). It was noted for its ability to alleviate symptoms such as fever, diarrhea, and vomiting. The famous medical book

Treatise on Fevers, written in 200 AD, also documented the use of Gegen Tang, a decoction made from kudzu root, for treating symptoms such as neck stiffness, reduced perspiration, and sensitivity to air drafts [7].

Kudzu flower (Gehua) was initially recorded as a remedy for alcohol intoxication, alcohol abuse, and dysentery. Puerarin is the primary biologically active compound found in the root of the kudzu plant. There are three primary dosage forms used in clinical applications: injectable, capsule, and tablet. In China, injection therapy is extensively employed for the management of many medical conditions such as angina pectoris, diabetes, retinal vein even artery blockage, cerebrovascular diseases, viral myocarditis, coronary heart disease, myocardial infarction, and sudden deafness. Puerarin is used in addition to other conventional drugs as an adjuvant treatment. The recommended daily dose is 400–600 mg for 10–15 days [8].

C. Rationale for reviewing Pueraria lobata's efficacy in lung cancer management

Puerarin, also known as daidzein 8-C-glucoside and chemically represented as C21H20C9, is a prominent isoflavonoid substance that is extracted from the herb Radix Puerariae. Past research has demonstrated that puerarin has advantageous impacts on cerebrovascular and cardiovascular diseases, such as coronary artery disease, heart failure, hypertension, and myocardial infarction. Furthermore, recent investigations have discovered that puerarin has an anticancer property against malignant cells [9]. It was discovered to suppress the proliferation of HT29 cells by augmenting the anti-proliferative properties of other anti-neoplastic drugs. The simultaneous administration of puerarin and 5-fluorouracil resulted in a combined antitumor impact that was greater than the sum of their individual effects in gastric cancer. Furthermore, puerarin suppressed cell proliferation and triggered programmed cell death in hepatocellular carcinoma cells and breast cancer [10]

Apoptosis is a prominent kind of programmed cell death characterized by a sequence of biochemical processes that result in distinct cellular changes, such as cell shrinkage, nuclear fragmentation, chromatin condensation, and chromosomal DNA fragmentation. Puerarin therapy exhibited a dose-dependent effect by dramatically augmenting the quantity of both early apoptotic cells and late apoptotic cells. Puerarin, a substance that inhibits cell proliferation, triggers programmed cell death (apoptosis) and cellular self-digestion (autophagy), has potential as a chemotherapeutic agent for lung cancer treatment [11].

II. Methodology

Search strategy

Using the keywords, a thorough search was carried out using the online databases of EBSCO, Cochrane, and MEDLINE/PubMed "Pueraria lobata", "kudzu," and "lung cancer". The filters applied Includes randomized controlled studies, controlled clinical trials, and clinical trials studies

(RCTs), human research, and the English language. We conducted a manual scan of the selected relevant papers' reference lists to find any possible further research.

Inclusion and exclusion criteria

The studies which are published after 2000 and are containing the keywords. Studies with inconsistent findings were excluded.

III. Pharmacological Properties of Pueraria lobata

A. Chemical composition and bioactive compounds

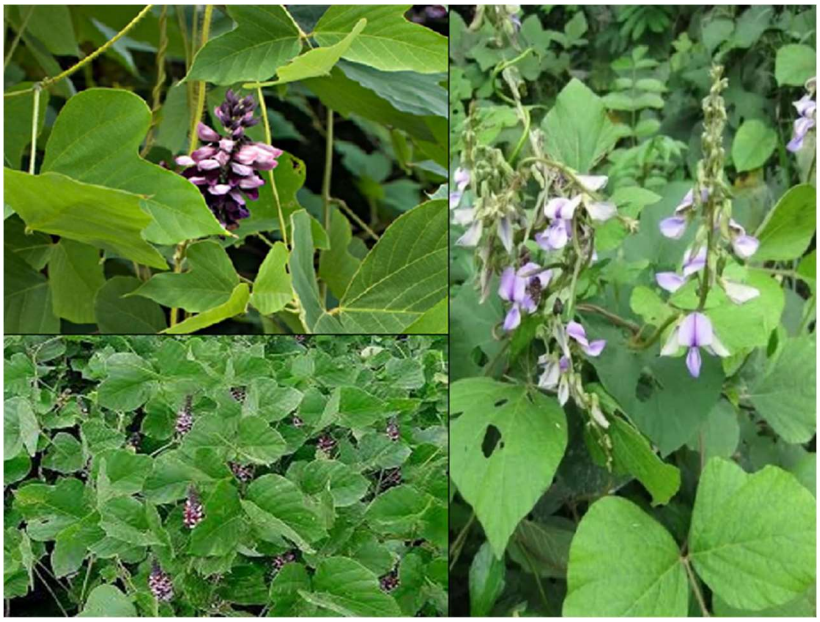

Figure 1: Kudzu in different places

Kudzu contains several active compounds such as daidzein, daidzin, Puerarin (daidzein-8-C-glucoside), biochanin A, 6-O-xyloglycitin, isoflavonoids, triterpenoids, tectoridin, glycitin, genistein, genistin, tectorigenin, and spinasterol [12].

Kudzu root is primarily composed of starch. The starch output from the fresh roots ranges from approximately 15% to 34.2%. The kudzu starch has a reported amylose concentration of 20.8–21% and an amylopectin chain length of 20.5. Furthermore, According to Kirakosyan et al. (2003), the refined starch that is taken out of the roots of kudzu plants and sold commercially is called kudzu starch and manufactured in Japan, lacks any significant amounts of isoflavonoids, except for trace amounts of daidzein [13].

Puerariae Flos, also known as P. lobata flowers range in color from reddish-purple to violet-purple. Usually, it blooms from the end of July into September. Due to its ability to enhance the elimination of acetaldehyde, it has frequently been utilized used in traditional eastern medicine as

a hangover cure. Puerariae Flos mostly consists of saponins, tryptophan derivatives, isoflavonoids, flavonoids, and phenolic chemicals. Puerariae Flos extracts and secondary metabolites have demonstrated promising pharmacological effects, including anti-diabetic, anti-inflammatory, property of anti-cancer, anti-endometriotic, estrogen-like, and sensitizing effects on paclitaxel-resistant ovarian cancer cells [12, 13].

A total of Using preparative thin-layer chromatography and column chromatography, fourteen chemicals were isolated in *Pueraria lobata* (Willd.) Ohwi. Spectroscopic examination was used to identify the structures for these compounds, which were then compared to previously published information in the literature. For the first time, a total of seven chemicals were extracted & recognized as *Pueraria lobata*. Among them are 3′,7-dihydroxyisoflavan, haginin A, ethyl ferulate, sandwicensin, isovanillin, linoleic acid, and isopterofuran substances found. The identities of the last ten compounds were determined with respect to their structure as follows: The compounds included are Coniferyl Aldehyde, Syringaldehyde, Genistein, β-sitosterol, luteinone, and luteol [16].

B. Mechanisms of action relevant to lung cancer treatment

Daidzein, biochanin A, and genistein all have cytotoxic qualities. According to preliminary study, genistein and biochanin A prevent stomach cancer cells from proliferating a laboratory setting by activating a signal transduction pathway that leads to apoptosis. Tectorigenin, a component, exhibited antiproliferative effects on HL-60 cancer cells by promoting cell differentiation and lowering the protein Bcl-2's expression, which prevents cell death. Research has examined the antiproliferative properties of tumor cell lines activity of Pueraria mirifica [14, 15].

Pueraria effectively reduces By upregulating the expression of M1 markers like inducible nitric oxide synthase (iNOS)+, CD197+, and CD40+ and downregulating the expression of M2 markers like CD163+, Arg-1+, and CD206+, it reduces the tumor volume and stops its development in the NSCLC xenograft model. Moreover, *Pueraria* enhances the production of tumor necrosis factor (TNF)-α, the pro-inflammatory cytokine interferon (IFN)-γ, as well as interleukin (IL)-12, while reducing the levels of transforming growth factor (TGF)-β, and the pro-tumor cytokines IL-4 and IL-10. The study by Kang et al. (2017) found that Pueraria can induce a transition converting polarized macrophages to the M2 phenotype, all without the assistance of additional auxiliary cells. Moreover, Pueraria blocks the invasion and movement of macrophages in lung cancer that is not small cell (NSCLC) and controls proteins that encourage the development of blood vessels that are new by blocking ERK translocation into the nucleus. Additionally, it prevents the MEK/ERK 1/2 pathways from being activated, which is responsible for cell signaling. IL-4 is known to stimulate the polarization of M2 macrophages and promote metastasis. However, Pueraria can counteract this effect by inhibiting the MEK/ERK1/2 pathway. Pueraria induces apoptosis by downregulating Bcl-2, resulting in upregulation of Bax. This activation of Caspase-3, 7, and 9 leads to cell death through apoptosis. In vivo, Pueraria effectively inhibits tumor growth [40].

IV. Preclinical Studies on Pueraria lobata in Lung Cancer

A. In vitro studies investigating anti-cancer effects

In 2023, Semenov A. L. et al. carried out research to assess the effects of a naturally occurring deep eutectic solvent (NADES) extract derived from Pueraria lobata roots, a plant rich in isoflavones (ISF), on a rat model for prostate cancer created by N-methyl-N-nitrosourea plus testosterone as well as an extract from Phaffia rhodozyma, that is rich in astaxanthin (ASX). Prior research has demonstrated the significant preventative benefits of a NADES extract derived from the roots of Pueraria lobata, which is abundant in isoflavones (ISF), in inhibiting the progression of A rat model of benign prostatic hyperplasia. Though the results have been conflicting and controversial, It has been determined that isoflavones are a significant dietary component in prostate cancer. The main ingredients of Pueraria lobata roots' isoflavone-rich NADES extract that were investigated are puerarin, daidzein, genistein, and formononetin, which possess anticancer effects. Anticancer activity has been demonstrated for all four isoflavones [17].

Ye Y et al., 2022 established both in vivo and in vitro models of ovarian cancer (OC) to assess the anticancer properties of puerarin. Puerarin was discovered to have an effective deterrent to the survival and growth of OC cells, while also inducing cell death. Puerarin therapy minimized the growth of tumors and controlled the gut for OC model mice flora. Furthermore, puerarin stimulated the activation of tumor suppressor genes both in vitro and in vivo [18].

Wang et al. assessed the therapeutic potential of puerarin nanosuspensions using the human colon cancer cell type HT-29 outdoors both in vitro (lab) and in vivo (live organism) settings. The effectiveness of puerarin nanosuspensions in treating cancer was shown in animals with HT-29 tumors. The cytotoxicity assay, morphological observation, Our preliminary investigation of apoptosis revealed the presence of puerarin nanosuspensions had a considerably enhanced ability to inhibit the growth of HT-29 cells were cultured vitro in contrast to the solution without puerarin. The evaluation of the generated puerarin nanosuspensions in vivo demonstrated superior anticancer effectiveness and reduced toxicity in comparison to the free solution [19]. Summary of the findings of anti-cancer effects have been given in details in Table 1.

Table 1: Findings of anti-cancer effects as concluded by the studies by In-vitro investigation

Study	Findings/Conclusion
Semenov A. L. et al. (2023)	Investigated the effects of a naturally occurring deep eutectic solvent (NADES) extract from Pueraria lobata roots on prostate cancer in rats. Found significant anticancer properties in isoflavones (ISF) such as puerarin, daidzein, genistein, and formononetin.

Ye Y et al. (2022)	Examined the anticancer properties of puerarin using in vivo and in vitro models of ovarian cancer. Discovered puerarin's efficacy in inhibiting tumor growth and inducing cell death, along with its ability to activate tumor suppressor genes.
Wang et al. (Year)	Assessed the therapeutic potential of puerarin nanosuspensions in human colon cancer cells (HT-29) both in vitro and in vivo. Found that puerarin nanosuspensions exhibited enhanced anticancer efficacy and reduced toxicity compared to free solutions.

B. Animal studies assessing efficacy and safety

In 2023, Song J et al. looked investigating the negative short- and long-term impacts of P. lobata & S. baicalensis root extract (HT047) in treating stroke in Sprague-Dawley rats, both female and male. The research offers proof of HT047's safety when used as an ischemic stroke therapy. Additionally, it demonstrates that in clinical practice, coupling P. lobata via S. baicalensis is safe [20].

In their 2015 study, Wang et al. investigated the hepatotoxic effects Effects kudzu extract from roots on mouse hepatocytes, HepG2 cells, and mice. The elevation of blood ALT and AST levels, along with observed histological alterations in the treated animals, indicates that kudzu root extract possesses hepatotoxic properties. The researchers determined that Kudzu root extract has the potential to cause liver damage, and therefore, caution should be exercised when using it [21].

Gao et al., 2016 examined the impact of an extract of kudzu root made of ethanol. They synthesized the extract and assessed its in vitro protective effect on human endothelial cells in the umbilical vein (HUVECs). The investigation found that a concentrated extract derived from kudzu root, which is high in isoflavonoids, has the capacity to protect endothelial cells in arteries against within-cell reactive oxygen species (ROS)-induced apoptosis and damage to mitochondria [22].

Hu et al. (2008) examined the therapeutic impact of Regarding non-small cells lung cancer (NSCLC), puterarin by studying its anticancer properties. The proliferation of NSCLC cell lines was dramatically suppressed by the administration of puerarin, as assessed by the CCK-8 kit inside an in vitro environment. The findings showed that puerarin exhibits anticancer properties and has the potential to be used as a treatment agent for lung cancer [23].

Table 2 shows the summary of the published studies' findings on the efficacy and safety of P. lobata on animal.

Table 2: Findings of the efficacy and safety of P. lobata on animal studies

Study	Findings/Conclusion
Song J et al. (2023)	Investigated the safety and efficacy of HT047, a combination of P. lobata & S. baicalensis root extract, in treating stroke in rats. Concluded HT047's safety for ischemic stroke therapy and the safety of coupling P. lobata via S. baicalensis in clinical practice.
Wang et al. (2015)	Examined the hepatotoxic effects of kudzu root extract on mouse hepatocytes, HepG2 cells, and mice. Identified elevation in liver enzymes and histological alterations, indicating potential liver damage. Caution advised in using kudzu root extract.
Gao et al. (2016)	Assessed the protective effect of kudzu root extract on human endothelial cells against reactive oxygen species (ROS)-induced apoptosis and mitochondrial damage. Found significant protection, suggesting potential cardiovascular benefits.
Hu et al. (2008)	Explored the therapeutic impact of puerarin on non-small cell lung cancer (NSCLC). Demonstrated significant suppression of NSCLC cell proliferation in vitro, suggesting puerarin's potential as a treatment agent for lung cancer.

V. Clinical Evidence of Pueraria lobata in Lung Cancer Management

Tam et al., (2009) assessed the effectiveness and security of Pueraria lobata (gegen) and Salvia miltiorrhiza (danshen) in preventing the recurrence of a condition. The supplementary treatment of D&G in individuals with coronary conditions was both efficient and well-tolerated in improving vascular structure and function [24].

In 2017, David Wing-Shing Cheung and his colleagues conducted a study to examine the effectiveness and safety of combining atorvastatin (AS) and DG (Danshen and Gegen) in treating hyperlipidemia generated by a high-fat diet. The results indicated that the combination of AS and DG had more potent hypolipidemic effects compared to AS or DG alone. In addition, DG may lessen the harmful effects from AS on the skeletal muscle and liver [25].

Aboushanab et al., 2022 conducted a study to Analyze the cytotoxic and antioxidant qualities of soy molasses (SM) and kudzu root (KR) extracts in relation to Pediatric solid tumors. The antioxidant activity in KR was substantially greater than in SM, which aligns with the observed cytotoxic action of KR & SM extracts on glioblastoma and osteosarcoma cells. Isoflavones were primarily responsible for the elevated flavonoid level and antioxidant capacity of the KR & SM extracts [26].

In their study, Chen et al. (2016) examined the effectiveness of puerarin 6″-O-xyloside (POS) in inhibiting tumor growth in the A549 cell line, which is a kind of human lung cancer. The study provided evidence of the potent antitumour effects of the POS. Reduced Bcl-2 levels and increased caspase-3, caspase-7, caspase-9, & Bax levels are linked to the processes [27].

Lee S et al., 2022 documented the instances of three Individuals suffering from late non-small cell cancer of the lung (NSCLC) were unable to continue traditional anticancer treatment. These patients were able to sustain a period of time without disease progression (progression-free survival or PFS) or recurrence (disease-free survival or DFS) and experienced improvement in symptoms following therapy using natural remedies. Only herbal remedies were used to heal patients remedies containing kudzu based on their medical condition and symptoms, without the use of conventional anticancer treatment. The study showcased the efficacy of herbal medicine as a viable treatment for suppressing tumor advancement and expansion progression-free survival (PFS) and disease-free survival (DFS) for individuals that has sophisticated non-small cells lung cancer (NSCLC) [28].
The studies mentioned above have contributed in the lung cancer management and their findings have been summarized in Table 3.

Table 3: Summary of the findings of clinical studies in Lung Cancer

Study	Findings/Conclusion
Tam et al. (2009)	Evaluated Pueraria lobata (gegen) and Salvia miltiorrhiza (danshen) in preventing condition recurrence. Found D&G supplementation in individuals with coronary conditions to be effective and well-tolerated, improving vascular structure and function.
David Wing-Shing Cheung et al. (2017)	Investigated the effectiveness and safety of combining atorvastatin (AS) and DG (Danshen and Gegen) in treating hyperlipidemia. Concluded that AS-DG combination had superior hypolipidemic effects compared to AS or DG alone, with potential reduction in AS-induced harmful effects on skeletal muscle and liver.

Aboushanab et al. (2022)	Analyzed cytotoxic and antioxidant properties of soy molasses (SM) and kudzu root (KR) extracts in pediatric solid tumors. Found KR extracts to have significantly higher antioxidant activity than SM, correlating with observed cytotoxic effects on glioblastoma and osteosarcoma cells. Isoflavones were identified as primary contributors to the elevated antioxidant capacity of KR extracts.
Chen et al. (2016)	Examined the effectiveness of puerarin 6″-O-xyloside (POS) in inhibiting tumor growth in A549 human lung cancer cells. Concluded that POS exhibited potent antitumor effects, evidenced by reduced Bcl-2 levels and increased caspase activity, suggesting its potential as a therapeutic agent for lung cancer.
Lee S et al. (2022)	Documented cases of late-stage NSCLC patients unable to continue traditional anticancer treatment, resorting to herbal remedies containing kudzu. Found these patients experienced prolonged periods without disease progression or recurrence, along with symptom improvement. Highlighted herbal medicine's efficacy as a viable treatment for suppressing tumor advancement and improving progression-free and disease-free survival in advanced NSCLC.

VI. Safety and Adverse Effects of Pueraria lobata

Safety:

1. Be cautious when administering to persons with hyperlipidemia or those using lipid medicines, as human study has revealed an increase in triglyceride levels [29].
2. Exercise caution when administering to those with gastrointestinal diseases or those who are taking gastrointestinal drugs, as it may cause digestive distress, including bloating, vomiting, dyspepsia, and nausea [29].
3. Exercise caution while administering kudzu to persons who consume alcohol, since it may lead to a disulfiram-like effect [30].
4. Exercise caution when administering to persons with hematologic problems or those who are using anticoagulants or antiplatelet medications, as it has been discovered that kudzu isoflavones have antagonistic action [31].
5. Exercise caution when administering puerarin to persons who are also taking benzodiazepines, as it may induce anxiety [32].

6. Exercise caution when administering to persons with hypertension or those taking hypotensive medications, as puerarin has been shown to lower heart rate and myocardial oxygen consumption in human studies [33].
7. Exercise caution when administering kudzu to persons who are also taking neurologic medications, as the daidzin compound in kudzu has the potential to impede the metabolism of serotonin and dopamine [34].
8. Exercise caution while administering puerarin to persons who are taking osteoporosis drugs, as it may inhibit the breakdown of bone tissue and stimulate the growth of new bone [35].
9. Exercise caution when administering kudzu to individuals who are also taking medications that have Kudzu may competitively impede the benefits of estrogen treatment because of its estrogenic action [36].
10. Exercise caution when administering daidzein to those who have arrhythmia or who use antiarrhythmic medications, as it could have antiarrhythmic effects [37].

Adverse effects:

Avoid if there is a confirmed hypersensitivity or allergy to Pueraria lobata, any of its ingredients, or any plants belonging to the Leguminoseae or Fabaceae family. An instance of case study was published that documented an allergic reaction in a patient who used a combination herbal treatment containing kudzu. The reaction manifested as a maculopapular outbreak that spreads from the thighs to the entire body. The administration of puerarin injection resulted in the rapid destruction of red blood cells within the blood vessels, known as acute intravascular hemolysis. Palpitations and chest pain were recorded in those who received Pueraria mirifica. A maculopapular drug eruption was observed following the use of a kudzu decoction. Individuals who received puerarin had symptoms such as headache, weariness, sleeplessness, and dizziness. Rats experienced hypothermia when puerarin or crude extracts of Pueraria lobata were administered intraperitoneally. Instances of patients experiencing cold symptoms and fever were observed in those who were administered puerarin [38].

VII. Discussion

One of the main causes of mortality worldwide and a serious public health problem is cancer worldwide. Although there has been remarkable advancement in cancer chemoprevention, there still exists a significant number of tumors for which therapy is insurmountably difficult methods. The extensive therapeutic properties of puerarin make it valuable in treating a wide range of health conditions. In this summary, we looked at puerarin's molecular targets and processes demonstrating has promise as a novel, effective anticancer medication for use in upcoming cancer treatments and prevention. Puerarin exhibits antitumor action via a number of methods, such as the suppression of the the overexpression of miR-16, caspase protein molecules, c-Jun N terminal kinase, extracellular signal-regulated kinase 1/2, and the NF-kB, mTOR, PI3K, and BCl-2

signaling pathways. These modifications lead to the suppression of cancer cell growth and/or the initiation of programmed cell death. Comprehending the molecular processes implicated might make it easier to conduct a more complete analysis of puerarin's potential for cancer treatment in chemotherapy and chemoprevention [39].

Isoflavones are a type of isoflavonoids that occur naturally in the plant family. Fabaceae predominantly exist as glycosides and many of them function as phytoestrogens within the bodies of mammals. According to a 2020 research by Ahmad et al., Poe has the ability to trigger apoptosis or programmed cell death, in a variety of cancer forms, including non-small cell lung cancers and colorectal (NSCLC), leukemic, breast, colon, gastric, and hepatocellular cancers [41].

Lung cancer (LC) is characterized by the development of highly malignant tumors, resulting in significant rates of morbidity and death. As a component of the microenvironment surrounding a tumor (TME), the microenvironment of tumor immune systems (TIME) is essential to the growth of tumors and immune system evasion system, and resistance to drugs. The TIME (Tumor Immune Microenvironment) consists of a variety of immune cells, immune cytokines, and other factors that play crucial roles in tumor progression and outcomes. An analysis examined the most recent scholarly articles and explored the potential applications of natural substances in controlling the body's internal clock, known as the circadian rhythm. Recent findings have demonstrated that the underlying processes of LC can be effectively addressed using natural substances through timely intervention, leading to a novel outlook and the possibility of developing therapeutic medications [42].

Puerarin's anticancer effects on non-small cells lung cancer (NSCLC) were investigated in a research. In vitro, the use of puerarin as a treatment significantly suppressed NSCLC cell line growth as measured using the CCK-8 kit. The results of the flow cytometry showed that puerarin treatments increased NSCLC apoptosis cells. The results indicated that puerarin exhibits anticancer properties and has the ability to treat lung cancer therapeutically [43].

Up to 50% of instances of primary tumors that spread to the central nervous system (CNS) are lung cancer patients. Recent developments in the management of brain metastases, such as novel radiation techniques, targeted drugs that are effective in the CNS, evidence supporting the use of immune checkpoint inhibitors, and strategies for managing leptomeningeal disease. Stereotactic radiology surgery (SRS) has proven to be a highly efficient form of radiotherapy, offering fewer adverse effects when in contrast to whole-brain radiation treatment (WBRT). Furthermore, drugs that inhibit tyrosine kinase (TKIs) of many generations with an overall CNS responses (ORR) varying from 70% to 80% are currently considered a recommended initial treatment for a specific group of advanced NSCLC patients who have identifiable molecular abnormalities that can be targeted [44].

Furthermore, although the central nervous system (CNS) was previously thought to be a place where the immune system is protected, there is increasing evidence indicating that immune checkpoint inhibitors (ICIs) can effectively stimulate long-lasting responses in brain metastases as well. Advancements in the management of non-small cell lung cancer (NSCLC) that has spread to the brain will rely on gaining a more comprehensive comprehension of the underlying biological mechanisms of central nervous system (CNS) metastases. Furthermore, it is necessary to enhance trial designs by intentionally incorporating outcomes that are specific to the central nervous system (CNS). Currently, several preclinical studies have explored the potential application of new agents to reduce metastasis. Additional current research focuses on identifying molecular changes that may be specifically linked to central nervous system metastases and could potentially be targeted for treatment. Hence, additional endeavors are required to ascertain alternative targets and therapies for metastases to the central nervous system of non-small cell lung cancer (NSCLC) [45].

Conclusion

The review provides a comprehensive examination of lung cancer, a leading cause of cancer-related mortality globally, emphasizing its prevalence, etiology, and treatment challenges. With smoking identified as the primary cause and significant disparities noted in smoking cessation efforts between developed and developing nations, the urgency for effective treatments is clear. Surgical excision followed by adjuvant therapy is recommended for early-stage Non Small Cell Lung Cancer (NSCLC), while chemotherapy or radiotherapy becomes the mainstay as the disease progresses. This review discussed into its traditional medicinal uses and pharmacological properties, particularly focusing on its active compounds like puerarin and its potential in cancer management. Pueraria lobata's therapeutic efficacy is explored through various preclinical and clinical studies, showcasing its ability to inhibit tumor growth and induce apoptosis in lung cancer cells. The mechanisms of action elucidated, including modulation of macrophage polarization and inhibition of cell signaling pathways, highlight its multifaceted potential as a chemotherapeutic agent.

The contribution of this review lies in its synthesis of existing research, offering insights into the pharmacological properties of Pueraria lobata and its potential role in lung cancer management. By collating evidence from in vitro, in vivo, and clinical studies, the review underscores the promising anticancer effects of Pueraria lobata, paving the way for further investigation and potential integration into conventional treatment protocols. However, caution is advised regarding safety considerations and potential adverse effects, necessitating careful patient selection and monitoring in clinical settings.

Therefore, this review can have clinical significance as clinicians can apply in their practice and researchers can use the findings for their further investigations. This review effectively brought forward the therapeutic potential of Pueraria lobata in the management of lung cancer, also sharing a public health concern globally. Further research and clinical trials are warranted to elucidate its

optimal dosage, efficacy, and safety profile, ultimately enhancing the armamentarium against this devastating disease.

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