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Review article

# Tobacco as bioenergy and medical plant for biofuels and bioproduction

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A B S T R A C T

Tobacco, a widely cultivated crop, has been extensively utilized by humans for an extended period. However, the tobacco industry generates a significant amount of organic waste, and the effective utilization of this tobacco waste has been limited. Currently, most tobacco waste is either recycled as reconstituted tobacco sheets or disposed of in landfills. However, tobacco possesses far more potential value than just these applications. This article provides an overview of the diverse uses of tobacco waste in agriculture, medicine, chemical engineering, and energy sectors. In the realm of agriculture, tobacco waste finds primary application as fertilizers and pesticides. In medical applications, the bioactive compounds present in tobacco are fully harnessed, resulting in the production of phenols, solanesol, polysaccharides, proteins, and even alkaloids. These bioactive compounds exhibit beneficial effects on human health. Additionally, the applications of tobacco waste in chemical engineering and energy sectors are centered around the utilization of lignocellulosic compounds and certain fuels. Chemical platform compounds derived from tobacco waste, as well as selected fuel sources, play a significant role in these areas. The rational utilization of tobacco waste represents a promising prospect, particularly in the present era when sustainable development is widely advocated. Moreover, this approach holds significant importance for enhancing energy utilization.

## 1. Introduction

Tobacco (*Nicotiana*) is a widely cultivated crop grown and ultilized in many countries around the world. However, the disposal of waste generated by the tobacco industry has not been handled in a rational manner. A significant portion of tobacco waste is typically treated through incineration or burial, leading to air pollution due to its high nicotine content. Moreover, such disposal methods can have detrimental effects on soil quality by damaging its structure [1,2].

Traditionally, tobacco waste has primarily been utilized for tobacco sheet production, where tobacco and tobacco waste are combined in specific ratios to manufacture cigarettes [3]. Additionally, tobacco waste is commonly employed as fertilizer and pesticide, requiring minimal processing and cost. However, it is crucial to note the importance of avoiding environmental pollution in

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these practices [1]. Tobacco contains approximately 4000 substances, comprising both particles and gases [4]. The main constituents encompass phenols, solanesol, polysaccharides, alkaloids, proteins, pigments, organic acids, minerals, among others [1,2]. Extracting these bioactive substances from tobacco holds significant value, as they have demonstrated various beneficial effects on human health and exhibit diverse biological functions in the prevention and treatment of different diseases [2]. For instance, phenols and solanesol present in tobacco possess notable biological activities, particularly in terms of their antioxidant capacity. Their health benefits encompass anti-aging properties, cancer prevention, cardiovascular disease prevention, among others. Even nicotine, considered harmful to human health, can be utilized as a medicinal component for Alzheimer's disease treatment [1,4]. Therefore, tobacco also holds importance in the medical industry. Furthermore, tobacco waste can be processed as biomass to generate high-value platform compounds vital to the chemical industry. This includes significant platform chemicals like 5-HMF, levulinic acid, and furfural [5], which can be further refined to produce various downstream energy products such as ethylene glycol and glycolic acid. Biomass derived from tobacco waste offers advantages over other energy sources, such as low cost, reduced pollution, widespread availability, and high recyclability [6–8].

In this paper, we will provide a comprehensive review of the utilization of tobacco waste in various fields, namely agriculture, medicine, chemical engineering, and energy. The first section will offer a concise overview of the applications of tobacco waste in agriculture. Subsequently, the second section will delve into the utilization of tobacco waste in medicine, with a particular emphasis on the existing research status of key extraction methods. The third section will outline the applications of tobacco waste in the chemical industry and energy sector. Finally, a summary of the tobacco waste utilization will be presented, accompanied by a future outlook.

## 2. Application of tobacco waste in agriculture

The agricultural applications of tobacco waste primarily involve its use as fertilizer and pesticide, as illustrated in Fig. 1(a). Tobacco contains essential fertilizer elements like phosphorus and potassium. By composting tobacco waste, harmful substances can be degraded, resulting in the production of pollution-free bioorganic fertilizer that meets the standards of green agricultural products [9], this composting method helps mitigate the pollution caused by organic waste [10]. Additionally, it reduces the production cost of biofertilizers and allows for the creation of specialized products tailored to the requirements of different crop varieties. Recent literature reports have highlighted the composting of tobacco waste. For example, composting tobacco waste and vegetable waste mixtures, along with biofortification using Brevibacillus (*Brevibacillus brevis*), demonstrated significant effectiveness in degrading harmful substances in tobacco. The resulting compost exhibited suitable element content for organic fertilization in agricultural production [11]. Zittel et al. composted tobacco waste with industrial effluent and observed substantial reductions in nicotine and heavy metal elements. The resulting compost had nitrogen, phosphorus, and potassium content ranging from 8.31% to 12.43%, meeting the maximum limits for heavy metal content and health standards for fertilizer use [12]. Another study composted a mixture of tobacco, wood chips, and various animal manures, a significant decrease occured in nicotine content from 12180 mg/kg to 160 mg/kg, and subsequent treatment improved crop yields [13]. Di et al. composted tobacco waste with agricultural soils, achieving a substantial increase in the relative abundance of beneficial microorganisms such as Pseudomonas (*Pseudomonas* sp.), Azotobacter (*Azotobacter* sp.), and Coprinus (*Coprinus* sp.), as well as a significant increase in effective nitrogen and potassium, while significantly reducing nicotine content [14]. Szwed and Bohacz used a compost formulated with a mixture of tobacco waste, bark, and straw to enhance gray-brown ash soils enriching elements such as nitrogen, phosphorus, and potassium, leading to a notable increase in maize

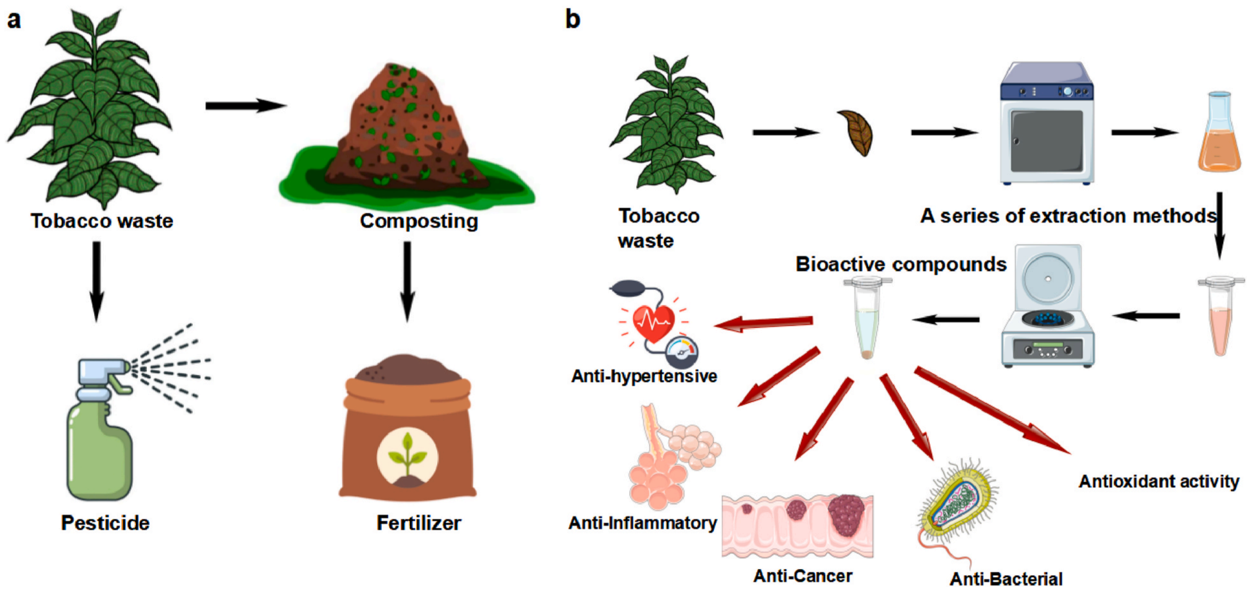


**Fig. 1.** Applications of tobacco waste in the a) agricultural and b) medical fields.

(*Zea mays* L.) yield [15]. Composting tobacco waste with various substances consistently meets fertilization standards, effectively addressing organic waste treatment issues associated with tobacco, while simultaneously improving the environment and efficiency.

Furthermore, tobacco waste can serve as a valuable resource for producing biopesticides, offering advantages that chemical insecticides do not possess. Improper use of chemical pesticides often leads to the development of resistance in pests. In contrast, biopesticides provide a means of pest control that reduces resistance while being environmentally friendly, making them a significant focus of research [16]. One prominent example is Bacillus thuringiensis (*Bacillus thuringiensis*), widely used for controlling the potato beetle (*Leptinotarsa decemlineata*), owing to its high specificity, easy degradation in the environment, and safety for humans, livestock and natural enemies of pests [17]. This bacterium exhibits insecticidal activity against tobacco beetle larvae, indicating its considerable potential for controlling tobacco pests in warehouse storage. Tobacco waste contains various natural insecticidal components, including tobacco alkaloids and essential oils. These components can be utilized to cultivate *Bacillus thuringiensis*, which was found to naturally exist in small quantities on tobacco leaf surfaces by Kaelin and Gadani [18]. This cultivation method possesses a dual insecticidal effect, as it allows for normal spore production while also utilizing the insecticidal properties of nicotine present in tobacco waste.

## 3. Applications of tobacco waste in the medical field

Tobacco harbors a plethora of biologically active compounds, which can be extracted using various techniques such as ultrasonic/microwave/high voltage discharge assisted extraction, supercritical extraction, high pressure liquid extraction, salting extraction, and heating precipitation extraction [1]. By combining traditional processes with modern extraction and separation methods like ultrasonic technique, different compounds can be extracted individually, maximizing the utilization of tobacco waste and obtaining relatively high extraction yields [19]. These bioactive compounds find significant applications in the medical field, as depicted in Fig. 1 (b). To exemplify, the applications and extraction methods of phenols, solanesol, polysaccharides, alkaloids, and proteins are detailed below.

### 3.1. Phenols

Phenols in tobacco exist in various forms, including free forms (glycosides), derivatives (acylated, esterified, and glycosylated glycosides), polymers, and oligomers [20]. Tobacco is known to contain high levels of polyphenols with antioxidant properties. The main polyphenols found in tobacco are chlorogenic acids and flavonoids as shown in Fig. 2(a) [21] and Fig. 2(b) [22], with approximately 400 species of chlorogenic acid identified [23]. These compounds exhibit various beneficial effects such as anti-oxidation, anti-inflammation [24], anticancer properties [25], blood pressure/blood sugar/blood lipid regulation, liver and gall-bladder nourishment [26], and scavenging of free radicals. Furthermore, they have been studied for their potential as antibacterial and

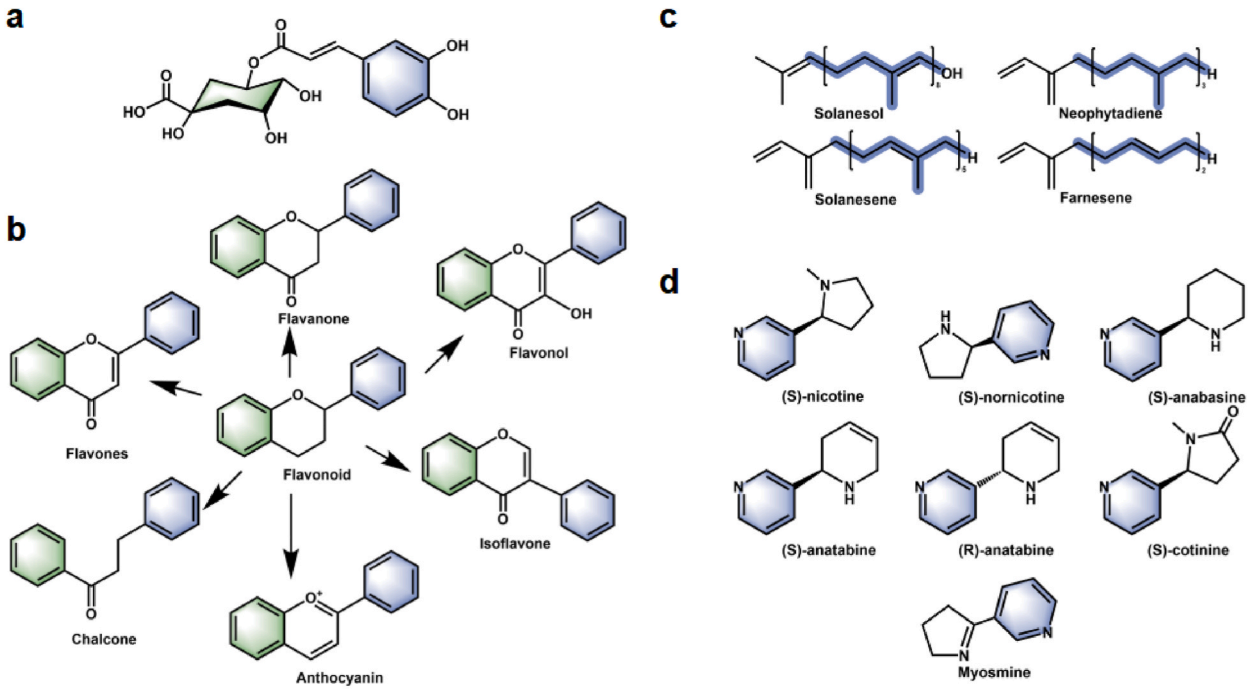


**Fig. 2.** Chemical structures: a) chlorogenic acid (5-O-caffeoylquinic acid); b) flavonoid; c) solanesol, solanesol analogues; d) nicotine. Adopted and reproduced with permission from ref [21,22,40,86].

antioxidant agents in food applications [21,27]. Chlorogenic acid, a prominent component of tobacco, is metabolized in the body primarily through the intestines and has shown positive effects on brain health and neurodegenerative diseases, including anti-depressant properties [28]. Zhang et al. discovered that chlorogenic acid can alleviate liver dysfunction caused by high L-carnitine intake, inhibit the formation of trimethylamine oxide, and improve the health of the intestinal flora [21]. Huang et al. found that chlorogenic acid significantly inhibits the increase of serum lipid levels and free fatty acids in the liver of mice (*Mus musculus*) [29]. Clinical trials conducted by Iwai et al. revealed the hypoglycemic effect of chlorogenic acid extracted from coffee beans (*Coffea*), demonstrating a significant reduction in blood glucose levels [30]. Although it did not have a significant effect on insulin levels, this suggests that chlorogenic acid may antagonize glucose transport [21]. In a study on hypertensive patients, Kozuma et al. found that chlorogenic acid exhibited hypotensive effects without significant adverse effects [31]. Chlorogenic acid is also a primary active ingredient in many herbal medicines, with honeysuckle (*Lonicera japonica*) and coffee beans being the main sources [32]. Extracting chlorogenic acid from tobacco waste could significantly improve its economic efficiency, and some preliminary studies have been conducted in this area. Wang et al. determined the content of chlorogenic acid (3-caffeoylquinic acid, 5-caffeoylquinic acid, 4-caffeoylquinic acid) and rutin in ten varieties of tobacco waste using High performance liquid chromatography with ultraviolet spectrophotometry(HPLC UV), with distribution ranges of 0.116–0.196%, 0.686–1.781%, 0.094–0.192%, and 0.413–0.998%, respectively [33], confirming the presence of chlorogenic acid in tobacco. Zeng et al. extracted chlorogenic acid from tobacco stems using double freeze-thaw ultrasonication, achieving an extraction rate of 0.502%, higher than conventional extraction and ultrasonication without pretreatment [25]. Banozic et al. performed high voltage electric discharge (HVED)-assisted extraction of chlorogenic acid from tobacco waste, demonstrating that HVED-assisted extraction outperformed conventional extraction in terms of free radical scavenging activity and chlorogenic acid content under the same process conditions [34]. Zhao et al. employed a macroporous resin to enrich and purify chlorogenic acid from tobacco waste, obtaining a product with 89.27% purity and a high yield [35]. These results suggest the feasibility of extracting chlorogenic acid from tobacco waste using auxiliary extraction methods, presenting significant value for its application in the medical industry and promoting a more rational utilization of tobacco waste

Flavonoids, another abundant group of phenolics in tobacco, possess a glycosylated structure, as depicted in Fig. 2(b). They are known to exhibit enhanced solubility, stability, and functionality compared with sapogenins [36]. Flavonoids have various beneficial effects, including anti-inflammatory, antibacterial, and even anticancer properties [37]. These effects can be attributed to their ability to inhibit pro-inflammatory cell signaling pathways and regulate genes involved in apoptosis, proliferation, metastasis, and angiogenesis, thereby preventing and treating cancer [22]. Through the extraction of flavonoids from tobacco, Ru et al. achieved a yield of $10.83 \pm 0.91$ mg/g and demonstrated that the extracting possesses scavenging effects on free radicals, indicating the potential of flavonoids as potent antioxidants [38].

Tobacco waste also contains other polyphenols, albeit in smaller quantities, including coumarins (such as scopoletin and its glycoside derivatives) and anthocyanins (such as anthocyanins-3-rutinoside, pelargonidin-3-rutinoside, and kaempferol) [39]. However, these compounds have received relatively less research attention and are less frequently reported.

### 3.2. Solanesol

Solanesol is an aliphatic terpene alcohol composed of nine isoprene units. It exists in both free and compound forms, with the free state being the predominant form. Its structural formula is depicted in Fig. 2(c) [40,41]. Solanesol is primarily found in solanaceous plants such as tobacco, tomato (*Solanum lycopersicum*), and potato (*Solanum tuberosum*) [40,42,43]. It possesses various medical properties, including antiulcer, antibacterial, antihypertensive, and anti-cancer effects [44,45]. Solanesol has even been reported to have efficacy in the treatment of acquired immune deficiency syndrome (AIDS) [40]. Moreover, it serves as a crucial raw material for the synthesis of coenzyme $Q_{10}$ and vitamin $K_2$ [40,42–44,46]. The antibacterial properties of solanesol have been investigated, revealing strong activity against both Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) bacteria [47]. Additionally, solanesol derived from tobacco has been shown to promote cell growth and enhance coenzyme $Q_{10}$ production [48]. Coenzyme $Q_{10}$ is an antioxidant dietary supplement with the effects of anti-inflammatory [49], anti-tumor [50,51], antihypertension, treating cardiovascular disease [52] and alleviating abnormal metabolic functions [53]. Coenzyme $Q_{10}$ has been documented to protect people from Parkinson's disease and other neurodegenerative diseases [54]. Sandor et al. found that coenzyme $Q_{10}$ significantly relieved migraine [55]. Vitamin $K_2$, another product synthesized from solanesol, plays a crucial role in blood clotting and has been found to prevent osteoporosis, inhibit cancer cell proliferation, and improve atherosclerosis [56,57]. In particular, many clinical studies have shown that vitamin $K_2$ can reduce the risk of developing some cancers, mainly through the induction of apoptosis and cell cycle arrest to inhibit cancer cells [57]. For example, vitamin $K_2$ has been reported to be effective in inducing apoptosis in leukemia cell lines HL-60 and U937 [58]. Intake of vitamin $K_2$ can reduce the risk of prostate, stomach, breast and lung cancers [51,57,59]. Vitamin $K_2$ can be obtained by Diels-Alder reaction after alkylation of solanesol bromide and anthraquinone derivatives, while solanesol bromide is obtained by bromination after purification of solanesol, so the amount of solanesol directly determines the amount of the product vitamin $K_2$. The primary source of solanesol is currently tobacco, and the efficient extraction of solanesol from tobacco is of great interest. Extraction methods such as microwave/ultrasonic-assisted extraction and supercritical extraction have been applied [1]. Machado et al. compared the extraction effects of microwave, ultrasound-assisted extraction, and conventional thermal reflux extraction, finding that the microwave method yielded the highest amount of solanesol with the lowest experimental dosage, recovering 30% of total solanesol from tobacco with a yield of 0.1% [46]. Wang et al. achieved higher purity of solanesol using the supercritical technique [60]. Additionally, Zhao and Du obtained a solanesol mixture with a purity of 26.8% using slow rotational counter-current chromatography (SRCCC), which has potential for industrial separation of solanesol using an SRCCC unit with a high-capacity column [61].

### 3.3. Polysaccharides

Polysaccharides, which are composed of interconnected monosaccharide residues through glycosidic bonds, constitute another significant component in tobacco [62]. They are primarily water-soluble and possess properties that allow them to act as thickeners, gelling agents, drug materials, drug releasers, and plasma substitutes due to their high osmotic pressure, viscosity, and water absorption [62,63]. Numerous studies have demonstrated that plant polysaccharides, including those from tobacco, exhibit diverse biological effects such as antitumor, immunomodulatory, hypoglycemic, lipid-lowering, anticoagulant, antioxidant, radioprotective, and antiviral activities [63–65]. Amagase et al. observed increased antioxidant markers after human trials involving polysaccharides derived from Lycium barbarum (*Lycium barbarum*) (LBP), further confirming their antioxidant potential [66]. The immunomodulatory effects of polysaccharides from Coriolus versicolor (*Coriolus versicolor (L.) Quel*) on nitric oxide production and various cytokines in mouse macrophages were reported by Lin et al. [67]. Notably, the antioxidant and immunomodulatory properties of polysaccharides have been suggested to contribute to their anticancer effects [68]. Several studies have demonstrated that polysaccharides inhibit the proliferation of liver cancer cells and induce apoptosis in a dose-dependent manner [69,70]. Furthermore, polysaccharides extracted from LBP have shown significant cell cycle blocking effects on gastric and colon cancer cells [71,72]. Polysaccharides have also exhibited hypoglycemic and lipid-lowering effects, protecting pancreatic islet cells from oxidative damage and improving cell survival [73–75]. Moreover, polysaccharide extracts have been found to promote the recovery of peripheral blood in mice with myelosuppression caused by radiotherapy or chemotherapy [76]. Tea polysaccharides have been shown to possess significant anticoagulant effects, providing potential references for stroke and myocarditis drugs [77]. It has been widely reported that polysaccharides including melon (*Cucumis melo*) polysaccharide, lactobacillus (*lactobacillus*) polysaccharide and coriolus versicolor polysaccharide can greatly inhibit viral replication [78], thus, it has an antiviral effect [79,80]. Tobacco leaves contain polysaccharides, with reducing polysaccharides comprising a significant proportion [81]. The quality of tobacco is even associated with its polysaccharide content [82]. Chemical composition analysis of tobacco waste polysaccharides reveals the presence of mannose, rhamnose, glucuronide, galacturonic acid, glucose, galactose, and arabinose [83]. Polysaccharides extracted from tobacco waste have demonstrated notable antioxidant activity and potential applications in the food and medical industries [82,84]. Other applications of tobacco polysaccharides have received limited research attention and present an important direction for the utilization of tobacco waste. Extraction methods for tobacco polysaccharides generally follow similar approaches to those used for phenols, including lyophilization and ultrasound-assisted extraction, resulting in relatively high yields [83,84]. It is worth mentioning that cellulose derived from tobacco holds significant potential for various chemical applications, which will be briefly discussed in the section on chemical applications.

### 3.4. Alkaloids

Tobacco contains several alkaloids, including nicotine, muscarine, atropine, quinine, morphine, and strychnine [1,85]. Among them, nicotine, also known as 3-(1-methyl-2-pyrrolidinyl) pyridine (Fig. 2(d) [86]), is the primary and most prominent alkaloid in tobacco [86]. It has been found that the total alkaloid content of tobacco is about 3.12%, and nicotine accounts for 2.53%. Nicotine is known to be harmful to the human body and highly addictive. However, it is also utilized in the production of nicotine patches and chewable tablets for smoking addiction cessation, which have shown remarkable effectiveness [87,88]. The principle behind these products is to provide a controlled dose of nicotine to alleviate withdrawal symptoms and assist individuals in overcoming their addiction. The nicotine dose is gradually reduced until the addiction is completely eliminated [87,88]. Some studies have suggested potential therapeutic applications of nicotine for the treatment of post-cerebral Parkinson's disease, Alzheimer's disease, and Tourette's syndrome [89]. However, it should be noted that the use of nicotine for these purposes remains controversial, as the lethal dose of nicotine is approximately 50 mg/kg for rats and 3 mg/kg for mice. In adults, a lethal dose is considered to be in the range of 40–60 mg [4].

### 3.5. Protein

Tobacco contains a significant amount of protein, with roasted tobacco containing approximately 10% protein and sun-cured

**Table 1**
Analysis of amino acid composition and content of tobacco protein [91].

| Compound | Sample | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Alanine | 0.18 | 0.13 | 0.08 | 0.17 | 0.15 | 0.17 | 0.23 | 0.2 | 0.16 |
| Glycine | 0.029 | 0.018 | 0.006 | 0.014 | 0.019 | 0.04 | 0.25 | 0.03 | 0.025 |
| Valinc | 0.08 | 0.03 | 0.05 | 0.07 | 0.05 | 0.05 | 0.06 | 0.07 | 0.05 |
| Leucine | 0.024 | 0.009 | 0.019 | 0.02 | 0.013 | 0.017 | 0.03 | 0.024 | 0.016 |
| Isoleucine | N.D.[a] | N.D. | 0.003 | 0.0027 | N.D. | N.D. | N.D. | N.D. | N.D. |
| Proline | 1.7 | 1.3 | 1.5 | 2.2 | 2.1 | 2.2 | 2.0 | 2.0 | 1.6 |
| Methionine | 0.0014 | N.D. | N.D. | 0.0021 | 0.001 | 0.001 | 0.0017 | 0.0017 | N.D. |
| Phenylalanine | 0.17 | N.D. | 0.15 | 0.15 | 0.11 | 0.12 | 0.17 | 0.14 | 0.11 |
| Tryptophan | 0.019 | 0.006 | 0.014 | 0.009 | 0.011 | 0.02 | 0.026 | 0.023 | 0.015 |

[a] N.D.-not detected.

tobacco and burley tobacco containing up to 20% protein [90]. The amino acid content of tobacco, which includes almost all essential amino acids for the human body, is shown in Table 1 [91]. If utilized properly, tobacco can serve as a high-quality protein source. Tobacco protein can be classified into soluble protein and insoluble protein, each accounting for half of the total protein content. The soluble protein can be precipitated by adding a 35% aqueous ammonium sulfate solution, resulting in the formation of two fractions: Fraction-I (F-1) and Fraction-II (F-2) [92]. F-1 protein contains a higher amount of essential amino acids compared with the Food and Agriculture Organization (FAO) standards for essential amino acid content in protein products. F-1 protein enriched with selenium exhibits stronger antioxidant effects. Selenium plays a vital role in the prevention and treatment of various diseases, such as Creutzfeldt-Jakob disease, macrosomia, cancer, and diabetes [93,94]. Tobacco selenium protein demonstrates low toxicity and high efficiency, making it a promising candidate for various applications [95,96]. Tobacco leaf protein possesses several advantageous characteristics, including high purity, low salt content, balanced amino acid composition, and higher nutritional value compared with general plant proteins. These properties make it particularly suitable for kidney and burn patients [97]. With the advancement of transgenic technology, tobacco protein finds broader applications. For instance, chloroplast-targeted transient expression in tobacco plants shows promise for the production of a cost-effective and effective HPV16 L1 VLP vaccine [98]. Other applications involve the expression of genes for the production of starch liquefaction enzymes, oral vaccines for fish, human interleukin-2 (HIL-2), H5N1 influenza virus vaccines, and exogenous proteins such as hepatitis surface antigen, cholera toxin B subunit, and Norwalk virus membrane protein [99–103].

Various methods can be employed for protein extraction, including heating precipitation, salting, membrane separation extraction, electrophoresis, and auxiliary extraction methods [104]. Ling et al. developed a macroporous amphiphilic ion exchange membrane using chitosan (CS) and carboxymethyl cellulose (CMC) to extract tobacco proteins. The membrane demonstrated the capability to obtain high-purity proteins that could be recycled [105]. Shi et al. utilized hollow fiber ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO) membranes to extract and desalinate tobacco proteins, achieving a maximum purity of 98.5% [106]. However, due to the presence of alkaloids in tobacco that are harmful to humans, effective methods to remove nicotine residues from proteins are necessary. Fu et al. successfully removed nicotine residues by rinsing tobacco proteins with an 85% phosphoric acid solution at pH 3.5, while maintaining a high protein recovery rate (94.5%) [107]. Additionally, double aqueous phase extraction has been widely employed for protein purification from various sources but may not be suitable for large-scale plant applications [108,109].

## 4. Applications of tobacco waste in the chemical industry and energy fields

### 4.1. *Lignocellulose*

As primary energy sources like coal and oil become depleted, there is a growing emphasis on alternative energy sources, and biomass energy, including lignocellulose, has garnered significant attention (Fig. 3) [110]. Lignocellulose is a high-quality biomass energy source comprising cellulose, hemicellulose, and lignin—the three main components of plant cell walls. Cellulose, represented by its basic structural unit of glucose linked by β-1,4-glycosidic bonds (Fig. 3) [111], is a linear polymer. Hemicellulose, on the other hand, is a heterogeneous polymer composed of xylose, arabinose, galactose, and other monomers (Fig. 3) [112]. Lignin contains benzene ring and phenolic hydroxyl group and other common functional groups, and has three basic structural units (Fig. 3) [113,114]. Lignocellulose possesses several advantages, including its low cost and renewable nature, making it an attractive material for research and applications in the medical, material, and chemical fields. Tobacco straw, in particular, contains a significant amount of lignocellulose. In the chemical industry, lignocellulose finds various applications, and the extraction methods for obtaining lignocellulose from tobacco are briefly discussed below.

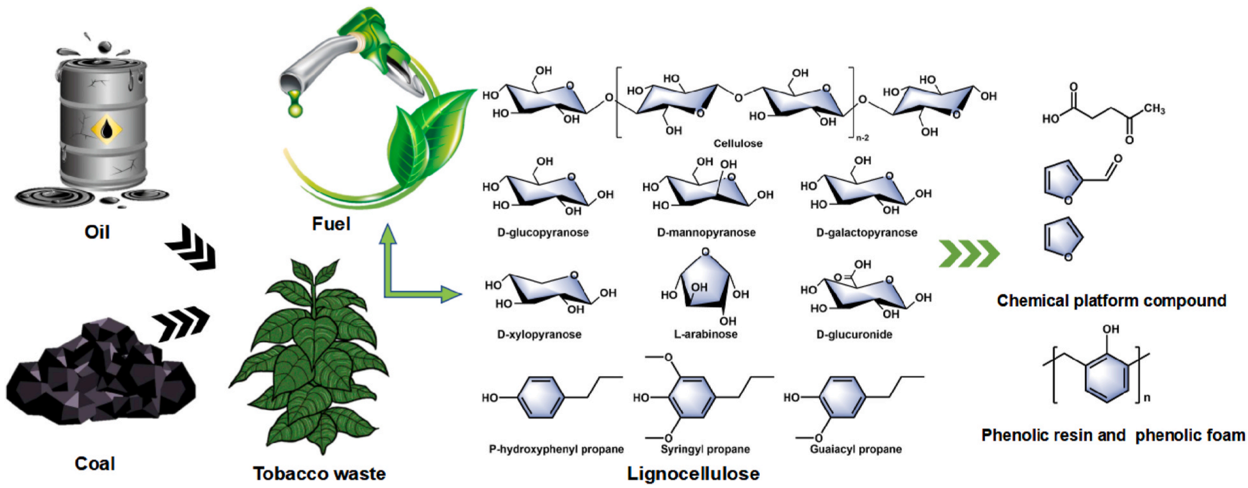


**Fig. 3.** Applications of tobacco waste in the chemical and energy fields. Adopted and reproduced with permission from ref [111,115].

Tobacco is rich in cellulose, which can be hydrolyzed and further processed to obtain levulinic acid—a significant chemical platform compound. Levulinic acid can undergo isomerization, dehydration, and further hydrolysis to produce compounds such as 1,4-pentanediol, γ-pentyl lactone, α-angelica lactone, 2-methyltetrahydrofuran and levulinate [116]. Another major component of lignocellulose, hemicellulose, yields pentose upon hydrolysis, which can be dehydrated using acid catalysts to produce furfural [117]. Furfural is an important chemical platform compound that can be converted into various downstream products, including furfuryl alcohol, furan, tetrahydrofuran, furan methylamine, furoic acid, levulinic acid, and used directly in the production of fungicides, nematicides, adhesives, flavor compounds, lubricants, and more [117,118]. Lignin, which accounts for approximately 2% of tobacco, is predominantly composed of guaiacyl propane units [119]. It can be utilized in the production of phenolic resin adhesives [115], nano carriers [120], phenolic foam and adsorbents. Phenolic foam derived from lignin, as a substitute for phenol, finds extensive use as a flame retardant material in chemical pipelines and high-rise buildings [121].

Various methods can be employed for the extraction of lignocellulose from tobacco. One common approach is to separate lignin from the overall structure of lignocellulose. Several methods used for tobacco lignin separation include the ionic liquid method, cellulose enzymatic hydrolysis, acid-base method, organic solvent method, supercritical extraction method, and ABS double aqueous phase extraction method [122,123]. Enzymatic hydrolysis offers mild conditions and high yields, but the purity of the initial product is relatively low, often requiring further purification [124,125]. The ionic liquid method has also been employed, with Fan et al. achieving an 85.38% lignin extraction yield and a purity of 90.21% using 1-ethyl-3-methylimidazolium diethyl phosphate [124]. Sun et al. utilized various treatments including freeze-drying, alkali pre-impregnation, ultrasound-assisted alkali pretreatment, ball-milling, and hydrothermal pretreatment to deconstruct tobacco straw and release lignin, finding hydrothermal pretreatment to be the most effective [125]. Currently, the main methods for separating and extracting cellulose and hemicellulose from tobacco include the dilute alkali method, heat treatment, dilute acid method with the assistance of microwave or ultrasonic techniques, and the emerging ionic liquid method [126–130]. The ionic liquid method, which leverages the interaction of anions and cations with cellulose hydroxyl groups to enhance cellulose solubility, has gained popularity [131]. Researchers such as Mohtar et al. and Lan et al. have successfully utilized the ionic liquid method to separate lignocellulose and achieve favorable yields [132,133]. Microwave-assisted hydrothermal method has been employed by Yuan et al. to extract cellulose and hemicellulose from tobacco biomass, resulting in a hemicellulose yield of 105.15 mg/g at 200 °C [134]. Luo et al. employed a combination of hot water/steaming pretreatment and cationic modification/homogenization to directly isolate desirable nanoscale cellulose from tobacco stems [135]. Furthermore, the efficiency of enzymatic hydrolysis can be enhanced by treating lignocellulose with acidified $FeCl_3$ [136,137]. Hemicellulose can be completely depolymerized by increasing the temperature to a specific level, taking advantage of its amorphous structure, which allows for easier separation from cellulose [138,139]. Optimal conditions are chosen to maximize cellulose retention and hemicellulose degradation [136].

### 4.2. Fuel

Tobacco waste can be effectively processed into various forms of fuels, including bio-coal, biogas and biofuel offering potential replacements for conventional energy sources. Bio-coal and bio-pellets derived from tobacco stalks can serve as alternative fuels to coal, while liquid smoke can be used as a substitute for chemical pesticides [140]. Xiao et al. conducted studies on biomass-based coal produced from tobacco waste and found that its performance during high-temperature curing was comparable to coal, with a higher burning rate. The energy efficiency of burning biomass coal ranged from 39% to 42%, surpassing that of coal combustion (36%) [141]. Exhaust gas testing by Hu et al. demonstrated that biomass-based coal exhibited significantly lower emissions of $CO_2$, CO, and $SO_2$ compared with coal combustion, with reductions of 57.28%, 95.45%, and 98.06%, respectively [142]. Cai et al. investigated the effects of hydrothermal carbonation on tobacco straw and found that it led to increased ignition temperature and energy density, transforming it into a high-energy solid fuel [143]. Liang et al. demonstrated that hydrothermal carbonization of tobacco waste catalyzed by trace amounts of graphene oxide produced hydrogen carbon with high energy density, indicating the feasibility of using hydrothermal reactions for solid fuel production [144]. Furthermore, tobacco waste can be utilized for the production of activated carbon, which has diverse applications. Chen et al. successfully produced high-performance activated carbons from tobacco waste using potassium hydroxide (KOH), potassium carbonate ($K_2CO_3$), and zinc chloride ($ZnCl_2$) as activating agents. The sample activated with $ZnCl_2$ exhibited a specific surface area of up to 1347 $m^2/g$, demonstrating good thermal stability [145].

There are also studies on using tobacco for the production of bio-oil and biogas. For example, Yan et al. employed a fluidized bed reactor to pyrolyze tobacco waste, such as leaves and stems, generating bio-oil containing aromatic compounds suitable for liquid fuel applications. The bio-oil yield from tobacco stems was 67.47%, higher than that from tobacco leaves, and the harmful components in the oil obtained from tobacco waste pyrolysis were lower compared with tobacco smoke, making it a potential resource for utilization [146]. Cardoso et al. conducted a comparative pyrolysis study of tobacco waste using zinc chloride and magnesium chloride as catalysts and found that the resulting bio-oil could be a valuable source of compounds, while the fuel oil obtained from the pyrolysis of tobacco waste with 10% zinc chloride exhibited good ignition properties [147]. Additionally, tobacco waste has the potential to generate biogas with a methane potential of 248 $Nm^3/Mg$ on average [148]. Utilizing tobacco waste as fuel offers significant benefits in the energy sector, finding applications in drying, baking agricultural products, and other energy fields, thereby enhancing energy and economic efficiency.

Recent advances in biofuel production have highlighted the potential of using tobacco as a lignin-rich substance. This involves green processing technologies that transform biological materials into biochemical products and biofuels. A novel approach, as proposed by Wang et al. integrates engineered bioenergy crops with yeast strains, employing green-like lignocellulose processes. This strategy aims for cost-effective bioethanol production and the generation of high-value bioproducts [149]. The process of enzymatic saccharification of biomass, a crucial step in biofuel and biological production, has been extensively studied. Following this, Zhang et al. made significant strides by identifying optimal biomass pretreatments for near-complete enzymatic saccharification. This enhances the overall yield of biofuel production and also opens avenues for producing valuable nanomaterials. Their research delves into the technological advancements in these pretreatments, showcasing their potential in generating highly valuable nanomaterials [150]. Furthermore, Zhang et al. studied characterizing length-reduced cellulose nanofibers in the natural rice fragile culm 16 (Osfc16) mutant. This mutant, defective in cellulose biosynthesis, was examined using both classic and advanced atomic force microscopy (AFM) techniques equipped with a single-molecular recognition system. By employing various cellulases, the study highlighted efficient enzymatic catalysis modes in the mutant, paving the way for precise engineering of cellulose substrates toward cost-effective biofuels and high-quality bioproducts [151]. In a related study, Zhang et al. utilized genetic engineering to modify cellulose nanofibrils, leading to the production of nanocrystals with remarkably reduced dimensions. These nanocrystals, derived from three knockout lines, serve as optimal intermediates for valuable bioproducts, significantly improving the efficiency of cellulose hydrolysis to fermentable sugar [152]. Lastly, Madadi et al. discovered that green proteins extracted from plants can act as active biosurfactants. These proteins not only enhance lignocellulose glycosylation but also effectively prevent lignin from releasing active cellulase, thereby enhancing biomass hydrolysis. Additionally, they participate in various chemical bindings with Cd, addressing key issues like high costs and low efficiency in biomass waste utilization [153]. In summary, these studies collectively demonstrate a paradigm shift in biofuel production, leveraging green processing technologies and genetic engineering. They underscore the potential of bioenergy crops, yeast strains, and genetically modified cellulose in creating efficient, cost-effective, and environmentally friendly biofuel and bioproducts.

### *4.3. Enzymes*

Various lignocellulosic residues, including tobacco waste, can be used as a carbon source for microorganisms in the production of enzymes, such as galacturonase, cellulase, etc. Solid state fermentation (SSF) is increasingly being used as a cost-effective technology for enzyme production and bioconversion of lignocellulosic waste biomass using cellulolytic microorganisms. Buntić et al. found that pretreatment of tobacco waste using Streptomyces CKS7 fermentation improved nicotine extraction and cellulase production [154]. Furthermore, Buntić et al. investigated the value addition of waste tobacco as lignocellulosic biomass for cellulase production by Rhizobium spp. of the genus Rhizobium chinense. For the first time, cellulases (Avicelase and carboxymethyl cellulase) were produced using Sinorhizobium meliloti strain 224 of Chinese root fungi during submerged and SSF using tobacco waste as substrate [155]. Utarti et al. studied 71 strains of actinomycetes using tobacco as a substrate, optimizing their cellulase production through SSF of tobacco stalks. The highest cellulase activity reached 0.40 mU/mL in actinomycete cultures, and further microscopic observations confirmed their classification as belonging to the genus Streptomyces [156]. There are also studies utilizing tobacco for the production of galactosidase. For example, Zheng et al. used immobilised Aspergillus oryzae to produce highly reactive endo- and exo-polygalacturonases (PGs) from tobacco industry wastewater. The addition of crude enzyme for hydrolysis of pectin-containing lignocellulosic biomass under high gravity conditions resulted in a 4.2-fold increase in glucose release compared to hydrolysis by cellulase alone. The process enables efficient production of pectin-degrading enzymes, provides a cost-effective method for tobacco wastewater treatment, and offers the possibility of obtaining high titres of fermentable sugars from pectin-containing lignocellulosic biomass [157]. Looking ahead, there is tremendous potential in utilizing tobacco for the production of enzymes such as cellulase and galactosidase. With the continuous advancement of biotechnology and processes, we can anticipate the emergence of more efficient and environmentally friendly production methods, leading to cost reduction and increased yields.

## 5. Summary and outlook

As mentioned previously, tobacco waste exhibits significant applications in various fields, including agriculture, medicine, chemical industry, and energy. In agriculture, tobacco waste can be utilized as fertilizers and pesticides, contributing to improved crop growth and pest control. In the pharmaceutical industry, the bioactive compounds present in tobacco offer potential health benefits, leading to their application in medical products. Furthermore, tobacco waste holds potential in the chemical industry for producing valuable chemical platform compounds derived from lignocellulose. In the energy sector, tobacco waste can be converted into fuel to provide an alternative energy source, or it can be used as a substrate for enzyme production. Despite these diverse applications, the current utilization of tobacco waste remains limited. Therefore, exploring better ways to utilize tobacco waste and promoting its industrialization present significant opportunities for future research and development.

## Ethics declaration

Review and/or approval by an ethics committee as well as informed consent was not required for this study because this literature review only used existing data from published studies and did not involve any direct experimentation/studies on living beings.

## Data availability statement

No data was used for the research described in the article.

## CRediT authorship contribution statement

**Kai Shen:** Writing – original draft, Validation, Methodology, Formal analysis. **Liwei Xia:** Writing – original draft, Validation, Methodology, Formal analysis. **Xiaoyuan Gao:** Validation, Methodology, Formal analysis, Data curation. **Cuiyu Li:** Validation, Methodology, Formal analysis, Data curation. **Ping Sun:** Validation, Methodology, Formal analysis, Data curation. **Yikuan Liu:** Validation, Software, Methodology, Formal analysis. **Hu Fan:** Validation, Methodology, Formal analysis. **Xu Li:** Validation, Methodology, Formal analysis. **Leyuan Han:** Validation, Methodology, Formal analysis. **Chengfei Lu:** Validation, Methodology, Formal analysis. **Kaixuan Jiao:** Validation, Methodology, Formal analysis. **Chen Xia:** Validation, Methodology, Formal analysis. **Zhi Wang:** Validation, Methodology, Formal analysis. **Bin Deng:** Validation, Methodology, Formal analysis. **Fanda Pan:** Writing – review & editing, Supervision, Resources. **Tulai Sun:** Writing – review & editing, Validation, Resources, Project administration, Conceptualization.

## Declaration of competing interest

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