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EXPLORING THE MEDICINAL AND THERAPEUTIC POTENTIAL OF AGRIMONIA PILOSA LEDEB: A COMPREHENSIVE REVIEW

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Abstract: Agrimonia pilosa Ledeb (APL) is an annual herb of the Rosaceae family, native to many parts of Asia, including China, Korea, and Japan. It has a long history of use in East Asian medicine for its medicinal properties. This review provides an overview of the botanical, phytochemical, and pharmacological properties of APL. Phytochemical components, flavonoids, tannins, triterpenes, and others indicate that plants have beneficial properties and are beneficial to human health, such as having many medicinal properties, including anticancer, antibacterial, antioxidant, and hepatoprotective properties. Additionally, the review provides details on the use of agrimony in herbal medicine, including its use in the treatment of diarrhea, inflammation, diabetes, and liver disease. APL is a wonderful plant with many medicinal properties, but more research is needed to understand its therapeutic potential, improve the extraction process, and elucidate the molecular mechanisms behind its activity.

IndexTerms **- Agrimonia Pilosa Ledeb, Natural medicine, Antioxidant, Anti-inflammatory, Antiviral, Anti-Cancer**

INTRODUCTION

The genus Agrimonia, which belongs to the Rosaceae family, has about a dozen species of perennial herbaceous flowering plants. These plants are mostly found in Northern Hemisphere temperate locations (Kato et al., 2010; Lee et al., 2018). Agrimonia pilosa Ledeb (AP) is one of these plants that is highly regarded in Chinese herbal medicine and is officially recognized by the Chinese Pharmacopoeia. (He et al., 2010; Lee et al., 2018). Agrimonia pilosa Ledeb (AP) has been extensively researched to investigate its potential therapeutic properties, taking into account its traditional medicinal use. Pharmacological studies have revealed a diverse array of beneficial effects linked to AP, encompassing anti-tumor, antiviral, antimicrobial, anti-hyperglycemic, antioxidant, and anti-inflammatory activities. (Lee et al., 2018). However, there is a notable gap in research regarding the toxicity profile of AP.

A recent study has uncovered several chemical classes contained in AP, with flavonoids and triterpenoids being important components. Specific flavonoid compounds, such as quercitrin, agriflavone, kaempferols, agripinols, and apigenin, have demonstrated varying bioactivities in vivo and in vitro and are recognized as the primary bioactive components of AP. Implementing quality control techniques based on these bioactive components is therefore critical to ensuring the efficacy and consistency of AP materials and associated products. However, it is worth noting that several countries and official pharmacopeias have yet to create standardized quality control standards for AP.

Several research has been conducted to measure the chemical composition of AP to acquire a better knowledge of its phytochemical profile (Lee et al., 2018). This study aims to give thorough information on the phytochemical and bioactive characteristics of AP by combining and assessing the available research. This collection will be a significant resource for future scientific inquiries and AP applications. This review aims to consolidate and evaluate the existing knowledge on the phytochemical and bioactive properties of AP, providing essential insights for further research and contemporary applications in various fields.

2. Plant Description: Taxonomic classification is

Kingdom: Plantae
Subkingdom: Viridiplantae
Infrakingdom: Streptophyta
Division: Tracheophyta
Subdivision: Spermatophytina
Infradivision: Angiospermae
Class: Magnoliopsida
Superorder: Rosanae
Order: Rosales
Family: Rosaceae
Genus: Agrimonia
Species: Agrimonia pilosa Ledeb (Le et al.,2018)

Fig,1- Agrimonia pilosa Ledeb

3. Traditional uses:

Agrimonia pilosa Ledeb. has been used to treat a variety of diseases in Korea and other Asian nations, including stomach discomfort, sore throat, headaches, bloody discharge, parasite infections, and dermatitis (Park et al., 2012; Kato et al., 2010). It is used as an astringent hemostatic drug in Austrian traditional medicine to treat bleeding, liver and bile diseases, and gastrointestinal and respiratory ailments (Vogl et al., 2013; Dhami et al., 2018). Root extract of this plant has been widely employed in Japan as a popular herbal remedy for cancer treatment. Furthermore, Agrimonia pilosa has a long history of use in China to treat conditions like diarrhea, gastric ulcers, inflammation, vision problems, detoxification, and promoting urine flow (Le et al., 2018; Xu et al., 2005). Additionally, it is recognized in Bulgaria and the United Kingdom for its anti-inflammatory qualities, and as an anti-parasitic agent in Korea. (Le et al., 2018; LG et al., 2014).

4. Phytochemistry:

The isolated compound of APL with their activity and MOA is tabulated below:

SI. No	Compounds	Activity	MOA
1	Quercetin	Anti-cancer	In human leukaemia U937 cells, quercetin has been shown to produce cell cycle arrest during G2/M (Tang et al.,2020).
2	Vitexin	Anti-Alzheimer	Cholinesterases (both AChE and BChE) and BACE enzymes are both inhibited by this compound (He et al.,2016; Choi et al.,2014)
3	Isoquercitrin	Anti-inflammatory	Anti-inflammatory effects of isoquercitrin were discovered by reducing the amounts of prostaglandin E2 generated by LPS-stimulated RAW264.7 cells (Valentova et al., 2014).
4	Quercitrin	Anti-microbial	Quercetin's antibacterial technique entails destroying bacteria's cell walls and modifying cell permeability, as well as regulating protein synthesis and expression, reducing enzyme activity, and inhibiting nucleic acid formation (yang et al.,2020).
5	Kaempferol	Anti-cancer	Apoptosis Phosphorylation of ERK and AKT, production of anti-apoptotic proteins XIAP and survivin, and depolarization of mitochondrial membrane potential are all instances of downregulation. Caspase-3 activity has increased. (Imran et al.,2019)
6	Rutin	Wound healing activity	When rutin, in the form of a hydrogel, was applied to skin lesions in rats, it resulted in a reduction in wound area when compared to control hydrogels. There was less oxidative stress in the wound

			region, as seen by lower lipid peroxidation and protein carbonyl concentration, as well as higher catalase activity (Almeida et al., 2012; Ganeshpurkar et al.,2016)
7	Apigenin	Anti-cancer	Breast cancer: reduced p-JAK1, p-JAK2, and p-STAT3 levels; elevated cleaved caspase-8, cleaved caspase-3, and PARP cleavage (Yan et al.,2017; Seo et al.,2015).
8	Luteolin	Anti-Hypertensive	The entire modeling impact of luteolin is partly due to the inhibition of VSMC proliferation and migration, which is due to the inhibition of the RAAS system, which results in a decrease in Ang II expression, as well as the regulation of ROS production and the MAPK pathway (su et al., 2015)
9	Hyperoside	Anti-nociceptive activity	Hyperoside has been found to have analgesic properties by lowering calcium (Ca2+) concentrations in afferent nerve terminals (Ku et al.,2014; Raza et al.,2017)
10	Agrimoniin	Anti-Diabetic	Strong-glucosidase and aldose reductase inhibitory activities (Grochowsk et al.,2018)
11	Kaempferol-3-0-α-L-rhamnopyranoside	Anti-viral	The compound is thought to have hindered viral particle receptors and impeded cell entry, resulting in less viral particle proliferation (Mehrbod et al.,2018)
12	Kaempferol-3-0-β-D-glucopyranoside	Anti-inflammatory	In response to lipopolysaccharide (LPS), inhibits the generation of nitric oxide (NO), prostaglandin E2, and interleukin (IL)-6 (Choung et al., 2017).
13	Kaempferol 7-0-β-D-glucoside	Anti-cancer	It can induce G2/M phase arrest in a dose- and time-dependent manner, with G2/M phase accumulation peaking at 24 h treatment and apoptotic sub-G1 phase accumulation significantly increasing after more than 24 h treatment (Fig. 6), implying cell cycle arrest followed by apoptosis as a sequential event (Xu et al., 2008).
14	Kaempferol 7-O-β-D-glucuronide	Anti-diabetic	Type 2 diabetes and obesity can be efficiently treated with PTP1B 538 inhibitors. The findings of the experiments showed kaempferol-7-O—D-glucuronide was an effective PTP1B inhibitor (Yue et al.,2019)
15	Kaempferol-3-0-β-D glucoside	Anti-inflammatory	The findings showed that inhibiting the NF-B and MAPK signalling pathways can reduce the levels of TNF, IL-1, and IL-6 following leptospira infection (Zhang et al., 2017).
16	Kaempferol 3-0-glucoside	Anti-bacterial	contact with extracellular proteins and bacterial cell walls, resulting in suppression of microbial growth (Taiwo et al.,2019)
17	Apigenin-7-O-β-Dglucuronide	Anti-inflammatory	Suppressing the AP-1 and MAPK signaling pathways in LPS-stimulated RAW 264.7 cells significantly decreased inflammatory responses by downregulating inflammatory-related gene expression (Hu et al., 2015).
18	Agriflavone	Anti- Alzheimer	PTP1B and AChE inhibitory activity (Nguyen et al.,2017)

19	Luteolin-7-0-β-d-glucopyranoside	Anti-HIV	Significantly suppressed the release of HBsAg and HBeAg in a dose-dependent manner (Tian et al., 2010).
20	Luteolin-7-0-β-d-glucoside	Anti-cancer	Carcinogen activation is blocked, carcinogen detoxification is increased, and error-free DNA repair is stimulated(Zemlicka et al.,2014)
21	Luteolin7-0-β-D-glucuronide	Anti-inflammatory	IL-6, iNOS, and COX-2 protein expression is inhibited. 2018 (Ma et al.)
22	Luteolin-7-0-β-d-glucuronide methyl ester	Anti-oxidant	To assess antioxidant activity, the ABTS+ radical cation (ABTS+) decolorization test was performed (Lee et al., 2010).
23	Tiliroside	Anti-Diabetic	In IR HepG2 cells, significantly increased AMPK activity decreased ACC activity, and increased glucose intake(Qin et al.,2011)
24	Aromadendrin	Inhibits T Cell Activation	There was a decrease in calcium (Ca2+) influx in activated T cells that had been pre-treated with aromadendrin. According to Western blotting, aromadendrin reduced the dephosphorylation and nuclear translocation of nuclear factor of activated T (NFAT) cells (Lee and Jeong 2020).
25	3-methoxy quercetin	Anti-inflammatory	There was a reduction in pro-inflammatory chemicals (NO and TNF-) as well as radical scavenging capacity against ROS and RNS in LPS-stimulated RAW 264.7 cells (Omeje et al., 2017).
26	Tormentic acid	Anti-tumor	As indicated by OA/PI staining, DNA laddering experiments, and an annexin V binding assay (Csuk et al.,2012), an apoptosis-inducing pathway is implicated.
27	Corosolic acid	Anti-diabetic	Enhanced glucose absorption in cells, impaired sucrose and starch hydrolysis, reduced gluconeogenesis, and lipid metabolism regulation(Miura et al.,2012)
28	Oleanolic acid	Hepatoprotective	Oleanolic acid has been shown to boost the nuclear accumulation of Nrf2, a major transcriptional regulator of antioxidant and detoxifying enzymes, culminating in the activation of Nrf2-dependent genes implicated in liver protection (Pollier et al., 2012).
29	Agrimophol	Anti-bacterial	When Mtb was subjected to acidic circumstances, Agrimophol coupled to Rv3852, a membrane-anchored, DNA-binding histone-like protein, was able to disrupt the bacterium's internal pH homeostasis and kill it (Mu et al.,2019; Zhao et al.,2015).
30	Esculetin	Neuro-protective	Bcl-2 expression is upregulated, Bax expression is downregulated, and caspase 3 is cleaved downstream. (Wang et al.,2012; Liang et al.,2017)
31	Esculin	Anti-inflammatory	Esculin reduced the levels of pro-inflammatory cytokines tumour necrosis factor (TNF-) and interleukin-6 (IL-6) in supernatant. Esculin significantly inhibited LPS-induced activation of the mitogen-activated protein kinase (MAPK) pathway in peritoneal macrophages (Niu et al 2015).

32	Ubelliferone	Anti-cancer	It was discovered that the activity was carried out via inducing apoptosis, cell cycle arrest, and DNA fragmentation(Ofentse Mazimba 2017; Yu et al2015)
33	Caffeic acid	Anti-hepatocarcinoma	CA works in hepatocarcinoma by limiting the production of reactive oxygen species (ROS), decreasing the oxidative stress that is so common in this illness (Espindola et al.,2019; Silva et al.,2014).
34	chlorogenic-acid	Anti-bacterial	Chlorogenic acid kills dangerous bacteria strains (Shigella dysenteria and Shigella pneumonia) by causing irreversible membrane permeability alterations, causing cells to lose their ability to maintain membrane potential and cytoplasm macromolecules such as nucleotides (Lou et al., 2011).
35	Ellagic acid	Anti-viral	suppresses the virus's replication by inhibiting HBx-induced transcriptional activation (Patkak et al.,2014; Nino et al.,2015)
36	Potentillin	Anti-cancer	It's worth noting that the host's immunological defense is aided by the activation of monocyte-macrophage and IL-I production. (Miyamoto et al.,1999)
37	Agritanin	Anti-diabetic	Against the PTP1B enzyme, agritannin has a substantial inhibitory effect(Nguyen et al.,2017)
38	Loliolide	Anti-inflammatory	Against the PTP1B enzyme, agritannin has a substantial inhibitory effect(Silva et al.,2021)
39	Afzelin	Anti-bacterial	The antibacterial activity of afzelin may be influenced by the hydroxyl and rhamnose groups, which may function as a negative and positive factor, respectively (Lee et al.,2014)
40	Apigenin7-0-β-d-glucoside	Anti-oxidant	The radical scavenging activities of ABTS, O2, DPPH, and OH were all substantial (Zhang et al., 2016).

5. Pharmacological activity:

5.1 Antiviral activity

According to Lee et al.,2021, active components ursolic acid (1), quercetin (2), and 1,2,3,4,6-penta-O-galloyl—D-glucose (3) of Agrimonia pilosa (AP), Galla whois (RG), and their combination (APRG64) reduced SARS-CoV-2 replication. In addition, SARS-CoV-2 and its variant (VUI-202012/01) demonstrated substantial binding affinity for the three chemicals (1, 2, and 3). As a result, APRG64 is a novel prospective antiviral drug for the treatment of COVID-19, and more clinical trials are needed.

5.2 Anti-Cancer

Hnit et al., 2021 discovered that Agrimol B, derived from Agrimonia pilosa Ledeb, may trap cancer cells in a G_0 state, revealing for the first time that agrimony B can change the quantities of regulators regulating the G_0 state.

5.3 Antinociceptive and Anti-Inflammatory

According to Feng et al.,2021, the molecular mechanism underlying the antinociceptive and anti-inflammatory effects of Mixed Agrimonia pilosa Ledeb. and Salvia miltiorrhiza Bunge Extract (ME) may include inhibition of pro-inflammatory cytokines, upregulation of anti-inflammatory cytokines, suppression of inflammatory mediators, and blocking of the MAPK signaling pathway. According to additional in vivo studies, It delays the course of ear edema in mice. ME, as a whole, might be a new source of comfort for arthritis patients.

5.4 Anti-bacterial activity

MRSA ATCC43300 was suppressed by a full flavonoid extract from A. pilosa Ledeb, with a MIC of 62.5 g/mL, according to He et al.,2022. MRSA's energy metabolism and protein synthesis were affected by the total flavonoid extracted from A. pilosa Ledeb.

5.5 Antioxidant activity

He et al.,2009 used four different testing methodologies to evaluate the antioxidant activity of a 95 percent ethanolic extract of Agrimonia pilosa produced by ultrasonically assisted extraction to that of Soxhlet extraction. Both the UEA (ultrasonically assisted extract of Agrimonia pilosa) and the SEA (Soxhlet extract of Agrimonia pilosa) extracts were shown to be rich in polyphenol and flavonoid components, as well as having significant antioxidant and free radical scavenging capabilities against DPPH and ABTS radicals. The antioxidant activity demonstrated by the test subjects was in the order UEASEA.

6. Agrimonia Pilosa Ledeb as a Source of Nutraceuticals

6.1. Use in Functional Foods and Beverages

Agrimonia Pilosa Ledeb can be found in functional foods and drinks, which are meant to boost health and well-being in addition to providing basic nutritional value. Its bioactive components, like as polyphenols and flavonoids, contribute to its antioxidant and anti-inflammatory properties, making it a desirable ingredient in a wide range of culinary applications. Agrimonia Pilosa Ledeb-infused functional foods and beverages may provide extra health advantages to consumers by improving immunological function, cardiovascular health, and general well-being.

6.2. Dietary Supplements and Health Products

Extracts or isolated components from Agrimonia Pilosa Ledeb can be used to formulate nutritional supplements and health products. These supplements may be offered in a variety of formats, such as capsules, pills, powders, or liquid extracts. By concentrating on the plant's beneficial bioactive components, these supplements provide a convenient and standardized approach for users to incorporate Agrimonia Pilosa Ledeb's potential health advantages into their daily routine. Common health products derived from this plant include immune support supplements, antioxidants, and formulations for promoting gastrointestinal health.

7. Agrimonia Pilosa Ledeb in Cosmeceuticals and Skincare

7.1. Role in Traditional Beauty Practices

For ages, Agrimonia Pilosa Ledeb has played an important part in traditional beauty practices around the world. This plant was often used in ancient Chinese, Korean, and Japanese beauty rituals for its alleged skin-enhancing effects. Agrimonia Pilosa Ledeb extracts and infusions have long been used in face masks, toners, and beauty elixirs to increase skin brightness, level skin tone, and counteract indications of aging. (Choi, et al., 2015). Historical texts and traditional remedies have extensively referenced the significance of Agrimonia Pilosa Ledeb in traditional skincare practices (Jeon, et al., 2018).

7.2. Emerging Trends in the Cosmeceutical Industry

As consumers seek natural and plant-derived ingredients in their skincare products, Agrimonia Pilosa Ledeb has emerged as a potential ingredient in the cosmeceutical market. Companies are exploring its incorporation into serums, creams, and masks to offer skincare products with additional benefits.

8. Conclusions:

In compiling the literature for this review, we considered the pharmacological characteristics, phytochemistry, traditional applications, and botanical description of AP. The plant has historically been utilized as an anti-inflammatory, antioxidant, anti-tumor, anti-diabetic, and anti-Alzheimer agent. Despite considerable advancements in the phytochemistry and pharmacology of AP, these results are quite preliminary. The existing research makes it clear that the principal components of AP are flavonoids, triterpenoids, phenols, and phenolic acids, which most likely have a substantial role in pharmacological activity. Additionally, it is crucial to evaluate any drug's toxicity, but curiously, no study has examined the toxicological consequences of AP. Therefore, in the future, thorough research will undoubtedly be needed to increase our understanding of the pharmacological effects, chemical composition, and effectiveness of AP as well as its bioactive components.

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