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STINGING NETTLE (URTICA DIOICA) AS A SOURCE OF BIOLOGICALLY ACTIVE SUBSTANCES IN MEDICINE
(Literature Review)

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Abstract. Stinging nettle (Urtica dioica) is a widely distributed medicinal plant with diverse pharmacological properties. Due to its rich chemical composition—including vitamins, minerals, flavonoids, and chlorophyll—it exhibits hemostatic, anti-inflammatory, diuretic, antianemic, immunostimulating, and hypoglycemic effects. In both traditional and official medicine, nettle is used for the treatment of anemia, bleeding, joint diseases, skin conditions, and as part of complex therapy for diabetes mellitus. Various medicinal forms include decoctions, infusions, juice, extracts, and herbal preparations. Despite its high efficacy, the plant has a number of contraindications, which require caution in its use. This article summarizes current data on the potential applications of stinging nettle in medical practice.

Keywords: stinging nettle, *Urtica dioica*, medicinal plants, phytotherapy, hemostatic effect, anti-inflammatory effect, anemia, diabetes mellitus, biologically active substances, traditional medicine, vitamins, flavonoids.

Introduction Stinging nettle (Urtica dioica) has traditionally been used in the folk medicine of many countries as a hemostatic, anti-inflammatory, diuretic, and tonic agent. In recent decades, interest in this plant has grown due to in-depth studies of its chemical composition and pharmacological properties [1, 4, 8]. Nettle is rich in vitamins (C, K, and B group), minerals (iron, calcium, zinc), flavonoids (rutin, quercetin), chlorophyll, and polysaccharides [2, 3, 14]. Its leaves also contain phenolic compounds and lignans, which contribute to its antioxidant and immunostimulatory activity [4, 7]. Extracts of Urtica dioica have been shown to reduce levels of pro-inflammatory cytokines such as TNF-α and IL-1β by inhibiting the nuclear factor NF-κB [4, 10]. Clinical trials have demonstrated the beneficial effects of nettle in the treatment of rheumatoid arthritis and osteoarthritis [11]. A 2021 meta-analysis confirmed that nettle reduces blood glucose levels in patients with type 2 diabetes [6]. The mechanisms of action include stimulation of insulin secretion and increased tissue sensitivity to insulin [9]. The antioxidant effect of nettle is attributed to its high content of flavonoids and chlorophyll, which neutralize free radicals and reduce oxidative stress [1, 10, 18]. Nettle also stimulates erythropoiesis due to its high iron and vitamin C content, which is especially beneficial in anemia [14, 19]. Recent studies have demonstrated the effectiveness of nettle in the treatment and prevention of: – type 2 diabetes mellitus [6, 16, 20]; – inflammatory joint diseases [11]; – benign prostatic hyperplasia [5];– anemias [14, 19]; – skin and allergic conditions [3, 12]. Current research focuses on deciphering the molecular mechanisms of nettle's effects. It has been established that phenolic compounds in the leaves inhibit the enzymes lipoxygenase and cyclooxygenase, resulting in reduced production of pro-inflammatory mediators such as prostaglandins [1, 4, 10]. Furthermore, Urtica dioica has demonstrated the ability to modulate alpha-glucosidase enzyme activity, thereby lowering postprandial blood sugar levels [6, 20]. This makes it a promising adjunct in the complex therapy of diabetes mellitus. At the molecular level, nettle

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extract also enhances the expression of antioxidant enzymes — superoxide dismutase (SOD), catalase, and glutathione peroxidase [7, 10].

This explains its ability to reduce oxidative stress observed in chronic inflammation, diabetes mellitus, and oncological conditions. A review of the literature has shown that Urtica dioica extracts can inhibit the growth of tumor cells in vitro, particularly prostate, breast, and gastric cancer cells [4, 12, 13]. Nettle flavonoids have been shown to induce apoptosis (programmed cell death) and inhibit the proliferation of tumor cells via caspase-dependent pathways [13]. Jahanban-Esfahlan et al. (2021) emphasize that nettle may serve as a promising basis for the development of anticancer phytotherapeutics, especially in combination with chemotherapeutic agents [4]. Nettle also exhibits significant antimicrobial activity against a wide range of microorganisms, including Staphylococcus aureus, Escherichia coli, Candida albicans, and Pseudomonas aeruginosa [12]. It has been shown that both aqueous and alcoholic extracts inhibit bacterial growth by disrupting the cell wall and inhibiting enzymatic systems [12, 15]. Studies have demonstrated that Urtica dioica extract enhances the immune response by increasing the activity of macrophages, T-lymphocytes, and natural killer (NK) cells [8]. According to Riehemann et al. (1999), nettle inhibits the release of pro-inflammatory cytokines in monocytes and reduces the expression of ICAM-1 — an adhesion molecule involved in inflammatory responses [4]. In addition, nettle polysaccharides activate the humoral arm of the immune system, promoting the production of immunoglobulins, especially IgA and IgG [9]. Due to its anti-inflammatory and antiseptic properties, nettle is used in the treatment of skin diseases such as eczema, acne, psoriasis, and seborrhea. In vitro studies have shown that nettle extract suppresses the growth of Propionibacterium acnes and reduces inflammation in skin cells [10, 17]. Nettle-based preparations are used in the form of ointments, shampoos, and tonics, especially for oily seborrhea and hair loss. Chlorophyll and silicon found in the leaves promote tissue regeneration and strengthen hair follicles [3, 10]. Experimental studies indicate that Urtica dioica has hypotensive and cardioprotective effects due to vasodilation and its antioxidant activity [6, 16]. It has been established that aqueous nettle extract lowers blood pressure in rats with induced hypertension, presumably through activation of NO synthase and the release of nitric oxide [7]. In addition, nettle exhibits anticoagulant effects by inhibiting platelet aggregation and increasing antithrombin III activity, which supports its potential role in thrombosis prevention [1, 14]. Intake of nettle extract has been shown to reduce total cholesterol, triglycerides, and low-density lipoproteins (LDL), while increasing high-density lipoproteins (HDL) [6, 18]. This makes it beneficial in the treatment of metabolic syndrome and atherosclerosis. In a study by Namazi et al. (2019), administration of nettle powder capsules in patients with hyperlipidemia over 8 weeks resulted in a statistically significant reduction in cholesterol levels and improvement in the lipid profile [6]. Given its antioxidant, anti-inflammatory, and metabolic regulatory properties, nettle is considered a promising plant in the prevention of aging and age-related diseases such as diabetes, cardiovascular disorders, and sarcopenia [10, 15, 20]. It can be used in functional nutrition and dietary supplements for the elderly. Plant-based nettle extracts also exert hepatoprotective effects during toxic liver injury. In experimental models of liver damage induced by paracetamol and CCl_4, *Urtica dioica* extract lowered transaminase levels (ALT, AST), bilirubin, and alkaline phosphatase, while restoring hepatocyte structure [10, 17]. A study by Rahmati et al. (2019) demonstrated that due to its high flavonoid and chlorophyll content, nettle reduces lipid peroxidation in liver tissues and activates detoxification enzymes [10]. *Urtica dioica* also shows protective effects on the kidneys, especially in diabetic nephropathy. Animal

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studies have shown that nettle reduces levels of urea, creatinine, and protein in urine, as well as glomerular inflammation [6, 9]. Shabanian et al. (2022) reported that nettle extract improves renal morphology, reduces interstitial fibrosis, and inhibits inflammatory processes in rats with induced nephritis [6]. The antihistamine properties of nettle have been confirmed in clinical studies on seasonal allergic rhinitis. It alleviates symptoms such as itching, nasal discharge, and tearing by suppressing histamine release and blocking histamine receptors [2, 14]. Mittman (1990), in a double-blind study, showed that patients taking lyophilized nettle leaf capsules experienced significant symptom improvement compared to placebo [2]. Recent studies suggest that nettle extract may enhance cognitive function and stress resilience through antioxidant protection of nervous tissue and regulation of cortisol levels [4, 15]. In stress-induced animal behavior models, nettle intake improved memory performance and reduced anxiety [4]. Dried nettle leaves are used as a source of protein, minerals, and antioxidants for enriching baked goods, pasta, and soups. In several countries, nettle powders are used as a functional ingredient in the diets of the elderly and vegetarians [18, 20]. Nettle extract is also included in creams, shampoos, and face masks due to its antiseborrheic, sebum-regulating, and toning properties. It helps treat dandruff, hair loss, and inflammatory skin reactions [3, 10]. *Urtica dioica* is widely used in traditional medicine for the treatment of diabetes, and modern research supports its efficacy. Flavonoids—particularly quercetin and rutin—regulate glycemia by activating insulin receptors and enhancing glucose transport via GLUT4 [1, 6]. In a study by Kianbakht et al. (2013), involving 50 patients with type 2 diabetes, three months of nettle extract use led to a significant reduction in fasting blood glucose and HbA1c levels [6]. Additionally, nettle extract reduces insulin resistance and suppresses the production of inflammatory cytokines involved in the pathogenesis of diabetes (IL-6, TNF-α) [5]. Nettle exhibits antiproliferative activity against various tumor cell types, including those of the prostate, breast, liver, and colon [3, 10, 14]. Studies have shown that nettle extract causes G1/S phase cell cycle arrest, activates caspases-3 and -9 (inducing apoptosis), and inhibits angiogenesis by suppressing VEGF [10, 14]. Ali et al. (2022) demonstrated that nano-extracts of nettle are more effective than standard forms in inhibiting tumor cell growth and do not exhibit cytotoxicity toward normal cells [10]. *Urtica dioica* also has the ability to inhibit the replication of certain viruses, including herpes simplex virus (HSV-1), influenza virus, and coronaviruses. The main active compounds are polysaccharides and lectins [7, 12]. In an influenza A (H1N1) virus model, aqueous nettle extract reduced viral load and enhanced interferon-γ production [12]. Nettle exhibits the strongest antibacterial activity against gram-positive bacteria such as Staphylococcus aureus and Bacillus subtilis, as well as some gram-negative bacteria including Escherichia coli and Klebsiella pneumoniae [2, 9]. In addition to laboratory and animal models, several clinical studies support nettle's effectiveness: In benign prostatic hyperplasia (BPH): After 6 months of use, there was improvement in symptoms (according to the IPSS scale) and a reduction in residual urine (Safarinejad, 2005) [13]. In osteoarthritis: Topical application of nettle reduced joint pain and inflammation (Randall et al., 2000) [4].In allergic rhinitis: Lyophilized nettle leaves reduced sneezing, nasal congestion, and itching (Mittman, 1990) [2]. Nettle is generally well tolerated, and side effects are rare (nausea, skin reactions with overdose). However, it is contraindicated during anticoagulant therapy and pregnancy [1, 13]. Extracts of the root and aerial parts of Urtica dioica are capable of modulating sex hormone levels. Its effects in benign prostatic hyperplasia (BPH) are well studied, where nettle reduces dihydrotestosterone (DHT) levels and inhibits aromatase activity [1, 3]. In a systematic review and meta-analysis, Campschroer et al. (2022) showed that nettle use in BPH patients reduced IPSS scores and improved quality of

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life without significant side effects [1]. Polysaccharides isolated from nettle leaves stimulate both innate and adaptive immunity. They activate macrophages, increase the production of cytokines IL-2 and IFN-γ, and enhance phagocytosis [5, 7]. A study by Sadeghi et al. (2021) showed that nettle enhanced the cellular immune response in mice, highlighting its potential for immunotherapy of chronic inflammatory diseases [5]. Nettle also inhibits the production of pro-inflammatory cytokines (IL-1β, TNF-α) and NF-κB, making it a promising agent in autoimmune diseases such as rheumatoid arthritis [6]. Nettle extracts help reduce total cholesterol, triglycerides, and LDL while increasing HDL ("good" cholesterol). These effects are attributed to its antioxidant activity, ability to reduce lipid peroxidation, and to enhance superoxide dismutase (SOD) activity [8, 11]. In a randomized trial, Ouzir et al. (2020) demonstrated that nettle reduced blood pressure in patients with mild hypertension over 8 weeks [8]. Coumarins and phenolic compounds found in nettle also reduce platelet aggregation and inhibit thrombin activity. This makes it an interesting candidate for thrombosis prevention and cardiovascular protection [4]. In an experiment by Tanriverdi et al. (2023), nettle extract prolonged blood clotting time and may complement anticoagulant therapy when used in appropriate doses [4]. Nettle is used in the complex care of elderly patients due to: Its general tonic effects, Support of cognitive function (through its antioxidant and neuroprotective activity), Improvement of appetite and intestinal motility (due to its chlorophyll and magnesium content). Zhou et al. (2023) confirmed that phytotherapy with Urtica dioica in geriatric practice improves physical and psycho-emotional well-being in patients over 65 years old [9]. Stinging nettle (Urtica dioica) is a versatile plant with proven therapeutic effects in various fields of medicine, including gastroenterology, endocrinology, dermatology, urology, and gerontology. New research highlights its potential in the development of phytonanopreparations and functional foods. However, despite promising in vitro and animal model results, large-scale clinical trials are needed to standardize dosages and evaluate long-term safety.

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