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POTENTIAL OF *MELILOTUS OFFICINALIS* AND CORN SILK AS ADJUNCT PHYTOTHERAPEUTIC AGENTS IN ENDOMETRIAL CANCER. A LITERATURE REVIEW

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Abstract: Abstract: Uterine cancer is one of the most significant gynecologic oncological problems, the relevance of which is increasing against the backdrop of an aging population, obesity, metabolic disorders, and molecular heterogeneity of tumors. This literature review evaluates the potential of sweet clover, or Melilotus officinalis (L.) Pall., and corn silk, known in pharmacognosy as Stigma maydis of the plant Zea mays L., as adjuvant phytotherapeutic agents for uterine cancer. The analysis shows that coumarins, flavonoids, and phenolic acids of sweet clover, as well as polyphenols, flavonoids, minerals, and polysaccharide fractions of corn silk have the potential to influence inflammation, oxidative stress, microcirculation, and metabolic disorders. However, the available data are insufficient to consider these plants as independent anticancer treatments. Their possible use should be considered only as a scientifically substantiated direction of maintenance therapy under the supervision of an oncologist and taking into account the risk of drug interactions.

Keywords: Endometrial cancer, uterine corpus cancer, *Melilotus officinalis*, qashqarbeda, corn silk, *Stigma maydis*, adjunct phytotherapy, inflammation, oxidative stress, supportive oncology.

QASHQARBEDA VA MAKKA POPUGINING BACHADON TANASI SARATONIDA YORDAMCHI FITOTERAPEVTIK VOSITA SIFATIDAGI IMKONIYATLARI. ADABIYOTLAR SHARHI

Annotatsiya: Bachadon tanasi saratoni ayollar reproduktiv tizimining muhim onkologik kasalliklaridan biri bo‘lib, uning dolzarbligi semizlik, metabolik buzilishlar, yosh omili va molekulyar geterogenlik bilan bog‘liq holda ortib bormoqda. Ushbu adabiyotlar sharhida qashqarbeda, ya’ni *Melilotus officinalis* (L.) Pall., hamda makka popugi, ya’ni *Zea mays* L. o‘simligining urg‘ochi gul ustunchalari va tumshuqchalari bo‘lgan *Stigma maydis*, bachadon tanasi saratonida yordamchi fitoterapevtik vosita sifatida baholandi. Tahlil natijalari qashqarbeda tarkibidagi kumarinlar, flavonoidlar va fenol kislotalar, makka popugidagi polifenollar, flavonoidlar, mineral moddalar va polisaxaridlar yallig‘lanish, oksidlovchi stress, mikrosirkulyatsiya va metabolik muvozanat bilan bog‘liq jarayonlarga ta’sir ko‘rsatishi mumkinligini ko‘rsatadi. Biroq mavjud dalillar bu o‘simliklarni mustaqil antisaraton davosi sifatida tavsiya qilish uchun yetarli emas. Ular faqat onkolog nazorati ostida, standart davolashga xalaqit bermaydigan yordamchi yo‘nalish sifatida ilmiy jihatdan o‘rganilishi mumkin.

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Kalit so‘zlar: Bachadon tanasi saratoni, endometrial saraton, qashqarbeda, *Melilotus officinalis*, makka popugi, *Stigma maydis*, yordamchi fitoterapiya, yallig‘lanish, oksidlovchi stress.

ВОЗМОЖНОСТИ ДОННИКА ЛЕКАРСТВЕННОГО И КУКУРУЗНЫХ РЫЛЕЦ КАК ВСПОМОГАТЕЛЬНЫХ ФИТОТЕРАПЕВТИЧЕСКИХ СРЕДСТВ ПРИ РАКЕ ТЕЛА МАТКИ. ОБЗОР ЛИТЕРАТУРЫ

Аннотация: Рак тела матки является одной из наиболее значимых онкогинекологических проблем, актуальность которой возрастает на фоне старения населения, ожирения, метаболических нарушений и молекулярной неоднородности опухолей. В данном обзоре литературы оценены возможности донника лекарственного, или *Melilotus officinalis* (L.) Pall., и кукурузных рылец, известных в фармакогнозии как *Stigma maydis* растения *Zea mays* L., в качестве вспомогательных фитотерапевтических средств при раке тела матки. Анализ показывает, что кумарины, флавоноиды и фенольные кислоты донника, а также полифенолы, флавоноиды, минеральные вещества и полисахаридные фракции кукурузных рылец потенциально могут влиять на воспаление, оксидативный стресс, микроциркуляцию и метаболические нарушения. Однако имеющихся данных недостаточно для рассмотрения этих растений как самостоятельного противоопухолевого лечения. Их возможное применение должно рассматриваться только как научно обоснованное направление поддерживающей терапии под контролем онколога и с учетом риска лекарственных взаимодействий.

Ключевые слова: Рак тела матки, рак эндометрия, донник лекарственный, *Melilotus officinalis*, кукурузные рыльца, *Stigma maydis*, вспомогательная фитотерапия, воспаление, окидативный стресс.

INTRODUCTION

Endometrial cancer, also referred to as cancer of the uterine corpus, is a malignancy arising predominantly from the epithelial lining of the uterus. It is clinically important because many cases are diagnosed at an early stage, yet aggressive molecular subtypes, recurrent disease, obesity-associated risk, and treatment-related complications continue to create a substantial burden for patients and health systems [1–5]. Contemporary oncology increasingly views endometrial cancer not only as a local gynecological disease but also as a biologically heterogeneous disorder shaped by hormonal, metabolic, inflammatory, genetic, and immune factors.

Modern treatment of endometrial cancer is based on histological type, stage, grade, lymphovascular invasion, molecular subtype, and patient-related factors. Surgical staging remains the main therapeutic foundation for many patients, while radiotherapy, chemotherapy, hormonal therapy, targeted treatment, immunotherapy, and clinical trials are used according to risk group and disease extent [3–5]. Therefore, any phytotherapeutic approach must be positioned only as supportive and adjunctive. It must not delay surgery, radiotherapy, systemic therapy, or evidence-based follow-up.

The growing interest in medicinal plants in oncology is related to several biological ideas. Many plant-derived compounds influence oxidative stress, inflammatory signaling, apoptosis, angiogenesis, glucose metabolism, and immune responses. These processes are relevant to cancer biology, although their modulation in cell culture or animal models does not automatically translate into clinical antitumor efficacy in humans [6–9]. This distinction is

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especially important in endometrial cancer, where molecular classification has shown that tumors may differ greatly in prognosis and treatment sensitivity [6].

Qashqarbeda is commonly associated with *Melilotus officinalis* (L.) Pall., a Fabaceae family plant known in English as yellow sweet clover and in Russian as донник лекарственный. Regional botanical literature also identifies medicinal qashqarbeda as *M. officinalis* [10]. The plant is rich in coumarins, flavonoids, phenolic acids, and other bioactive compounds. Experimental studies describe antioxidant, anti-inflammatory, anticoagulant, anti-edematous, and cytotoxic activities, although direct clinical evidence in endometrial cancer is absent [11–13].

Makka popugi, or corn silk, is the stigma and style of *Zea mays* L., pharmacognostically known as *Stigma maydis*. Corn silk has traditionally been used in urinary and metabolic conditions, and recent reviews describe flavonoids, polyphenols, phenolic acids, polysaccharides, minerals, and other constituents with antioxidant, anti-inflammatory, diuretic, antihyperglycemic, and lipid-modulating properties [14–16]. These effects may be relevant to supportive oncology, particularly because metabolic syndrome, obesity, chronic inflammation, and oxidative stress are closely linked with endometrial cancer risk and survivorship.

The aim of this review is to evaluate the scientific rationale, potential mechanisms, safety considerations, and research perspectives for using *M. officinalis* and corn silk as adjunct phytotherapeutic candidates in endometrial cancer.

MATERIALS AND METHODS

This article was prepared as a narrative literature review. Scientific publications were considered from PubMed, Google Scholar, MDPI full-text archives, NCBI Bookshelf, IARC Global Cancer Observatory materials, and accessible clinical guideline sources. The search covered literature on endometrial cancer epidemiology, molecular classification, oxidative stress, inflammation, PI3K/AKT signaling, phytochemistry of *Melilotus officinalis*, pharmacological properties of corn silk, and safety issues related to coumarin-containing products.

The following search terms were used in different combinations. The search included “endometrial cancer,” “uterine corpus cancer,” “molecular classification,” “oxidative stress,” “inflammation,” “PI3K AKT pathway,” “natural products,” “Melilotus officinalis,” “sweet clover,” “coumarin,” “corn silk,” “Stigma maydis,” “Zea mays,” “flavonoids,” “polyphenols,” “anti-inflammatory,” “antioxidant,” and “adjunct phytotherapy.”

Priority was given to international cancer statistics, clinical guidelines, systematic or narrative reviews, experimental studies with clearly described phytochemical and pharmacological findings, and safety-focused publications. Sources were excluded when they made unsupported claims of cancer cure, lacked identifiable authorship, did not describe methods, or presented non-scientific promotional information.

The level of evidence was interpreted cautiously. Clinical guidelines and cancer statistics were treated as high-level contextual sources. Human clinical data specific to endometrial cancer and these two plants were considered the most relevant but were not found. In vitro and animal studies were used only to formulate mechanistic hypotheses and research directions.

RESULTS

General evidence landscape - The literature shows a clear gap between traditional use and cancer-specific clinical evidence. Both *M. officinalis* and corn silk contain biologically active compounds that may influence mechanisms relevant to cancer biology, but there are no convincing clinical trials proving therapeutic efficacy against endometrial cancer. Their current role is best understood as a possible supportive and investigational direction.

Table 1. Evidence framework used for evaluating the two plant materials

Evidence	*Melilotus officinalis*	Corn silk, *Stigma maydis*	Relevance to

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domain			endometrial cancer
Botanical identity	Medicinal qashqarbeda, yellow sweet clover, Fabaceae family	Stigma and style of *Zea mays* L.	Correct identification is essential for safety and reproducibility
Main phytochemical groups	Coumarins, flavonoids, phenolic acids, alkaloid-related compounds	Flavonoids, maysin derivatives, polyphenols, phenolic acids, minerals, polysaccharides	These groups may affect oxidative stress and inflammation
Main experimental effects	Antioxidant, anti-inflammatory, anticoagulant, anti-edematous, cytotoxic activities	Antioxidant, anti-inflammatory, diuretic, metabolic, possible cytoprotective activities	Potential supportive relevance, not direct proof of anticancer efficacy
Human cancer-specific evidence	Insufficient for endometrial cancer	Insufficient for endometrial cancer	Clinical use as anticancer therapy is not justified
Safety priority	Bleeding risk, anticoagulant interaction, possible hepatotoxicity in susceptible patients	Diuretic and metabolic effects, possible interaction with diuretics, antihypertensive, antidiabetic, and anticoagulant therapy	Supervision is necessary in oncology patients

Phytochemical and biological profile of *Melilotus officinalis* - *Melilotus officinalis* contains coumarin and related compounds, flavonoids such as quercetin and luteolin derivatives, phenolic acids including caffeic and salicylic acid derivatives, and other polar secondary metabolites [11–13]. Liu and colleagues isolated several compounds from the aerial parts of *M. officinalis* and reported antioxidant, anti-inflammatory, and antitumor-related activities in experimental models [12]. A recent review of sweet clover also emphasized phenolic compounds, coumarin, and antioxidant activity as key pharmacological features of the genus [11].

The theoretical relevance of *M. officinalis* in endometrial cancer is linked to three mechanisms. The first is modulation of oxidative stress. Cancer cells are characterized by altered redox metabolism, and oxidative stress can influence apoptosis, autophagy, DNA damage responses, migration, and cell-cycle progression [7,8]. The second mechanism is inflammatory regulation. Chronic inflammation contributes to tumor-promoting microenvironments, metabolic disturbance, and tissue remodeling. The third mechanism is vascular and lymphatic support. Sweet clover preparations have historically been discussed in relation to edema and venous or lymphatic circulation, which may be relevant to supportive care but not to direct tumor eradication.

However, coumarin-containing plants require particular caution. Coumarin and coumarin derivatives are pharmacologically active, and their metabolism differs among individuals. Literature on coumarin-induced hepatotoxicity indicates that most patients tolerate coumarin, but a small subset may develop mild to moderate hepatotoxicity [17]. In addition, herbal products with anticoagulant or antiplatelet effects may increase bleeding risk when combined with anticoagulants, antiplatelet agents, perioperative treatment, thrombocytopenia, or liver disease [18].

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Phytochemical and biological profile of corn silk - Corn silk is a nutritionally and pharmacologically interesting plant material containing carbohydrates, proteins, vitamins, minerals, mucilage, fibers, polyphenols, flavonoids, ascorbate, and other antioxidant compounds [14–16]. Studies report that corn silk powder and extracts contain measurable total phenolic and flavonoid content, with antioxidant activity demonstrated through DPPH, ABTS, and FRAP assays [15]. A 2024 narrative review described corn silk as a source of flavonoids, polyphenols, phenolic acids, fatty acids, terpenoids, and other bioactive substances with anti-inflammatory, antioxidant, antihyperlipidemic, antihypertensive, and glucose-regulating effects [14].

In the context of endometrial cancer, corn silk may be relevant mainly through supportive mechanisms. Because obesity, insulin resistance, dyslipidemia, and chronic low-grade inflammation are associated with endometrial cancer risk and survivorship, a plant material with metabolic and antioxidant activity may deserve further investigation [3,14–16]. Its traditional diuretic use may also be relevant to supportive symptom management, although oncology patients require careful monitoring of hydration, electrolytes, renal function, and concomitant medications.

Corn silk should not be interpreted as a proven anticancer agent for uterine corpus cancer. The evidence is predominantly preclinical and pharmacognostic. The most reasonable scientific hypothesis is that standardized corn silk extracts may influence inflammatory and oxidative pathways that are indirectly relevant to cancer-associated metabolic and supportive care.

Table 2. Main phytochemical groups and possible mechanistic relevance

Plant material	**Key constituents**	**Experimentally described biological effects**	**Possible relevance in adjunctive care**	**Main limitation**
Melilotus officinalis	Coumarin, flavonoids, phenolic acids, salicylic acid derivatives, caffeic acid derivatives	Antioxidant, anti-inflammatory, anticoagulant, anti-edematous, cytotoxic activity in experimental studies	May support research on inflammatory and oxidative pathways, microcirculation, and postoperative edema	No direct clinical proof in endometrial cancer; safety concerns with bleeding and liver function
Corn silk	Flavonoids, maysin derivatives, polyphenols, phenolic acids, minerals, polysaccharides	Antioxidant, anti-inflammatory, diuretic, antihyperglycemic, lipid-modulating effects	May support research on metabolic inflammation, oxidative stress, urinary comfort, and quality of life	No validated antitumor efficacy in uterine corpus cancer
Combined research model	Phenolic and flavonoid-rich plant matrix	Potential complementary antioxidant and anti-inflammatory activity	Could be studied as a standardized supportive formulation	Unknown pharmacokinetics, unknown interactions, no clinical trials

Biological relevance to endometrial cancer pathways - Endometrial cancer development and progression involve interactions among estrogen exposure, obesity, insulin resistance,

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inflammation, genetic mutations, epigenetic changes, immune surveillance, and altered redox metabolism [3,6–9]. The TCGA molecular classification divided endometrial carcinoma into biologically meaningful groups, including POLE-ultramutated, microsatellite instability hypermutated, copy-number low, and copy-number high serous-like tumors [6]. This classification confirms that a single supportive phytotherapeutic approach cannot be expected to act uniformly across all endometrial cancer subtypes.

The PI3K/AKT pathway is particularly relevant because PTEN loss and PI3K pathway alterations are frequent in endometrioid endometrial carcinoma [6–8]. Oxidative stress and PI3K/AKT signaling are interconnected, and natural products may modulate these processes in experimental systems [7,8]. Nevertheless, these mechanistic observations should be translated carefully. Antioxidant effects can be beneficial in reducing oxidative damage, but excessive or poorly timed antioxidant supplementation may theoretically interfere with therapies that rely partly on oxidative stress to damage tumor cells. This is one reason why unsupervised use of strong plant extracts during chemotherapy or radiotherapy is not recommended.

Table 3. Potential supportive targets and level of evidence

Supportive target	Relevance in endometrial cancer	Possible plant-related rationale	Evidence strength
Oxidative stress	Involved in DNA damage, apoptosis, treatment response, and metabolic inflammation	Both plants contain phenolic and flavonoid compounds with antioxidant activity	Moderate preclinical rationale, weak clinical evidence
Chronic inflammation	Linked with obesity, metabolic syndrome, tumor microenvironment, and survivorship burden	Anti-inflammatory activity reported for *M. officinalis* and corn silk extracts	Moderate preclinical rationale, weak cancer-specific evidence
Metabolic dysregulation	Obesity, diabetes, insulin resistance, and dyslipidemia influence risk and outcomes	Corn silk has reported glucose- and lipid-modulating effects in experimental studies	Promising but clinically unproven for cancer outcomes
Edema and microcirculation	Relevant after surgery, lymph node assessment, radiotherapy, or vascular comorbidity	Sweet clover has traditional and pharmacological association with edema and circulation	Supportive hypothesis only; safety must be prioritized
Quality of life	Fatigue, urinary discomfort, inflammation, and metabolic symptoms affect survivorship	Corn silk and sweet clover may be studied in supportive care protocols	Requires controlled clinical trials

Safety considerations

Safety is central when discussing phytotherapy in cancer patients. Endometrial cancer patients may undergo surgery, radiotherapy, chemotherapy, hormonal therapy, immunotherapy, anticoagulation for thromboembolic risk, analgesic treatment, and management of diabetes or hypertension. Plant extracts may interact with these treatments.

Melilotus officinalis deserves special caution because of coumarin-related pharmacology. It should not be used without medical supervision in patients receiving anticoagulants, antiplatelet drugs, non-steroidal anti-inflammatory drugs with bleeding risk, perioperative treatment, liver disease, thrombocytopenia, or unexplained bleeding. Coumarin hepatotoxicity is uncommon but

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clinically relevant in susceptible individuals [17]. Herbal anticoagulant interactions have also been discussed in the broader literature on herb–drug interactions [18].

Corn silk is generally discussed as a mild diuretic and metabolic plant material, but this does not make it automatically safe for oncology patients. It may theoretically influence fluid balance, potassium status, glucose levels, blood pressure, and the effect of diuretics, antihypertensive drugs, antidiabetic therapy, or anticoagulants. Standardization is another problem because the amount of active compounds depends on plant variety, growing conditions, harvesting time, drying, extraction solvent, and storage.

Table 4. Practical safety questions before any clinical research or supervised adjunctive use

Safety question	Why it matters
Is the plant material botanically verified?	Misidentification may cause ineffective or unsafe use
Is the extract standardized?	Variable coumarin, flavonoid, and polyphenol content changes biological effects
Is the patient receiving anticoagulants or antiplatelet therapy?	*M. officinalis* may increase bleeding-related concerns
Is there liver disease or abnormal liver enzymes?	Coumarin-related hepatotoxicity is possible in susceptible individuals
Is the patient receiving chemotherapy or radiotherapy?	Antioxidant-rich products may theoretically influence treatment response
Are diabetes, hypertension, kidney disease, or diuretic therapy present?	Corn silk may affect fluid, electrolyte, glucose, or blood pressure balance
Is the goal supportive rather than antitumor treatment?	These plants are not proven replacements for evidence-based oncology

DISCUSSION

The review indicates that *M. officinalis* and corn silk are scientifically interesting but clinically unproven adjunct phytotherapeutic candidates in endometrial cancer. Their relevance is strongest at the level of biological plausibility. Both contain compounds capable of influencing oxidative stress and inflammation, while corn silk additionally has metabolic and diuretic properties and *M. officinalis* has vascular and anti-edematous pharmacological associations.

The most appropriate interpretation is not that these plants “treat” endometrial cancer, but that they may help generate research hypotheses for supportive oncology. In practical terms, future studies could examine whether standardized extracts influence inflammatory markers, oxidative stress biomarkers, metabolic parameters, postoperative edema, urinary symptoms, fatigue, and patient-reported quality of life. These endpoints are more realistic and ethically appropriate than claiming direct tumor regression without clinical evidence.

The mechanistic relationship with endometrial cancer is biologically plausible because obesity-associated inflammation, insulin resistance, estrogenic stimulation, PTEN/PI3K/AKT pathway alteration, and redox imbalance are relevant to endometrial carcinogenesis [3,6–8]. Natural products that modulate these pathways may be useful research tools. However, the same biological complexity also creates risk. A compound that is antioxidant in one context may be pro-oxidant or treatment-interfering in another. A plant that improves microcirculation may increase bleeding risk in a postoperative or anticoagulated patient. A diuretic plant may be harmless for one person but problematic for another with kidney disease or electrolyte imbalance.

For *M. officinalis*, the major advantage is the presence of biologically active coumarins and flavonoids with anti-inflammatory and antioxidant activity [11–13]. The major concern is the

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same coumarin-related pharmacology that makes the plant active. Oncology patients often have increased thrombotic and bleeding risks, and many receive perioperative anticoagulation or drugs affecting hemostasis. Therefore, *M. officinalis* is not a casual herbal tea recommendation in this population. It requires standardization, dose control, liver monitoring in research settings, and careful exclusion criteria.

For corn silk, the main advantage is its broad phytochemical profile and relatively strong pharmacognostic literature describing antioxidant and anti-inflammatory effects [14–16]. Its metabolic relevance may be important because metabolic syndrome and obesity are important in endometrial cancer risk and survivorship [3]. The main limitation is the lack of cancer-specific human evidence. Corn silk may be safer than coumarin-rich plants in some settings, but it still requires attention to diuretic, glucose-lowering, blood pressure, renal, and electrolyte-related effects.

A scientifically responsible research program could begin with phytochemical standardization of locally collected qashqarbeda and corn silk. The next stage would include in vitro testing on endometrial cancer cell lines representing different molecular backgrounds, such as hormone-sensitive endometrioid models and more aggressive non-endometrioid models. Outcomes should include cell viability, apoptosis, migration, oxidative stress markers, inflammatory cytokines, PI3K/AKT/mTOR signaling, estrogen receptor expression, and interaction with standard drugs. Only after safety and mechanistic clarity should animal studies or small human supportive-care trials be considered.

Clinical trials should not be designed to replace standard therapy. Instead, they could test whether a standardized formulation improves postoperative recovery, inflammatory status, metabolic parameters, urinary comfort, or quality of life when used under oncological supervision. Such trials must include strict monitoring for bleeding, liver enzymes, renal function, electrolytes, glucose, and drug interactions.

CONCLUSION

Melilotus officinalis and corn silk have phytochemical and pharmacological properties that justify scientific interest as adjunctive, supportive, and investigational agents in endometrial cancer care. Their potential relevance is related mainly to antioxidant, anti-inflammatory, metabolic, vascular, and quality-of-life pathways. Current evidence does not support their use as independent anticancer treatment and does not justify replacing surgery, radiotherapy, chemotherapy, hormonal therapy, targeted therapy, immunotherapy, or guideline-based follow-up.

The most balanced conclusion is that qashqarbeda and makka popugi may be considered promising research candidates for supportive oncology, but their clinical use must be cautious, standardized, individualized, and supervised by qualified healthcare professionals. The next scientific step should be phytochemical standardization, mechanistic testing in endometrial cancer models, safety assessment, and carefully designed clinical studies focused on supportive outcomes rather than unsupported claims of tumor cure.

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