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REVIEW ARTCILE

Cimicifuga racemosa (L.) Nutt.: Pharmacological Effects, Using Areas and Current Clinical Data

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***Cimicifuga racemosa* (L.) Nutt.: Pharmacological Effects, Using Areas and Current Clinical Data**

SUMMARY

Cimicifuga racemosa (L.) Nutt., also known as "black cohosh", is a perennial herbaceous plant that has been widely used, particularly for its effects on physiological and neuroendocrine processes. This review aims to present a comprehensive evaluation of the pharmacological properties, active constituents, and current clinical data related to C. racemosa extracts. Bioactive components such as triterpene glycosides, phenolic acids, and flavonoids found in the plant contribute to its anti-inflammatory, antioxidant, and neuroregulatory effects. Studies have reported its potential to alleviate symptoms such as vasomotor disturbances, mood alterations, and sleep disorders. Although promising, the exact mechanisms of action remain under investigation, and further well-designed randomized clinical studies are needed to clarify its therapeutic role and ensure long-term safety.

Keywords: *Cimicifuga racemosa, medicinal plants, pharmacological profile, clinical efficacy.*

***Cimicifuga racemosa* (L.) Nutt.: Farmakolojik Etkileri, Kullanım Alanları ve Güncel Klinik Veriler**

ÖZ

"Kara kohoş" olarak da bilinen Cimicifuga racemosa (L.) Nutt., özellikle fizyolojik ve nöroendokrin süreçler üzerindeki etkileri nedeniyle yaygın olarak kullanılan çok yıllık otsu bir bitkidir. Bu derleme, C. racemosa'nın farmakolojik özellikleri, aktif bileşenleri ve mevcut klinik verileri hakkında kapsamlı bir değerlendirme sunmayı amaçlamaktadır. Bitkide bulunan triterpen glikozitler, fenolik asitler ve flavonoitler gibi biyoaktif bileşenler, bitkinin antienflamatuar, antioksidan ve nöroregülatör etkilerine katkıda bulunur. Çalışmalar, bitkinin vazomotor bozukluklar, ruh hali değişiklikleri ve uyku bozuklukları gibi semptomları hafifletme potansiyelini ortaya koymuştur. Bu sonuçlar umut verici olmasına rağmen, bitkinin kesin etki mekanizmaları halen araştırılmaktadır. Ayrıca bitkinin terapötik rolünü açıklığa kavuşturmak ve uzun vadeli güvenliğini sağlamak için iyi tasarlanmış randomize klinik çalışmaların yapılması gerekmektedir.

Anahtar Kelimeler: *Cimicifuga racemosa, tıbbi bitkiler, farmakolojik profil, klinik etkinlik.*

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INTRODUCTION

Black cohosh, also known as *Cimicifuga racemosa* (L.) Nutt. (syn. *Actaea racemosa* L.), has traditionally been used in North American ethnomedicine for gynaecological disorders, musculoskeletal pain, and inflammatory conditions. Phytochemical analyses demonstrate a complex profile of metabolites, including triterpene glycosides (e.g., actein, 27-deoxyactein), phenolic derivatives, flavonoids, tannins, and minor volatile constituents (Burdette et al., 2002), suggesting multiple pharmacodynamic targets. Preclinical findings indicate anti-inflammatory, antioxidant, and neuromodulatory activities, alongside possible oestrogen-modulating effects (Liske et al., 2002). Clinical studies suggest benefits for vasomotor symptoms, mood, anxiety, and sleep, but methodological heterogeneity limits interpretation of results (Mahady et al., 2005). Extracted materials differ significantly, leading to inconsistent pharmacological profiles. This hinders comparative effectiveness and the establishment of dose–response relationships. Safety concerns necessitate a critical appraisal of existing data. Although not definitively causal, conflicting findings highlight the need for more integrated evaluation (Naser et al., 2011a). A comprehensive review is required on black cohosh in complementary medicine due to its growing global use, since existing reviews focus on menopausal symptoms, and mechanistic aspects are often overlooked. The present review integrates preclinical and clinical evidence to clarify knowledge gaps and identify priority areas for future research for a robust *C. racemosa* evidence-based framework.

Botanical features

C. racemosa is a perennial, herbaceous, and rhizome plant belonging to the Ranunculaceae family (Flora of North America Editorial Committee, 2009). Although the height of the plant varies between 1.5 and 2.5 meters on average, it can grow taller under suitable ecological conditions (Foster & Duke, 2000). Underground organs, especially thick, irregularly branched, and fibrous rhizomes, constitute the most valuable parts of this plant from a medical point of view. Its rhizomes contain high levels of triterpene glycosides and some other phytochemical compounds (Jiang et al., 2008). The stem of the plant is erect, hollow, and often fragile, which is interpreted as part of the plant's adaptation to humid and shady forest environments (Moerman, 1998).

The leaves are arranged in a spiral shape on the upper parts of the plant, compound in structure, and usually divided into palmate or pinnate. The leaf margins are distinctly dentate, and the leaf surface is often hairy (Flora of North America Editorial Committee, 2009). In summer, the plant forms flowers of the frequent racemose type, white in color, with a characteristic appearance (Foster & Duke, 2000). As an important morphological feature, petals are absent in flowers; instead, the bright white color and transparent staminodes give the flower a distinctive appearance.

C. racemosa reproduces vegetatively, mostly through rhizomes, and rarely reproduces by seed. It usually takes several years for its seeds to germinate and for the plant to reach full maturity, revealing that the species has a slow-growing biological profile (Moerman, 1998). For this reason, rhizomes form a rich nutrient store for the survival of the plant, especially in competitive habitat conditions in the natural environment (Flora of North America Editorial Committee, 2009).

Figure 1. General appearance of *C. racemosa* (U.S. Forest Service, 2019)

Figure 2. Appearance of *C. racemosa* flowers

National Center for Complementary and Integrative Health. (2024, January 5). Black cohosh. U.S. Department of Health and Human Services. https://www.nccih.nih.gov/health/black-cohosh

Figure 3. Appearance of *C. racemosa* fruits

Board of Trustees of the Royal Botanic Gardens, Kew. (n.d.). Actaea racemosa: Images & distribution. Plants of the World Online. Retrieved February 18, 2026, from https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:316204-2/images

Distribution area and ecological characteristics

C. racemosa is a plant that is widely distributed in North America and especially in the eastern and southeastern regions of the United States (Foster et al., 2000). It is also distributed in moist, shady, and densely forested ecosystems along the Appalachian Mountain range (U.S. Forest Service, 2019). The plant prefers humus-rich, well-drained soils with high organic matter, often thrives in underforest vegetation, in the shade of trees, and grows more efficiently in cool, humid microclimates (Moerman, 1998). However, due to increased medical and commercial demand, regressions due to overgathering have been observed in some local populations, which have negatively affected the conservation status of the species (Wagner et al., 2010). In this regard, *C. racemosa* is among the "species at risk" in some regional nature conservation programs, with emphasis on sustainable harvesting practices (Kaiser, 1997). In recent years, controlled cultivation practices have increasingly been adopted to reduce pressure on natural populations of *C. racemosa*, alongside growing efforts to preserve

ecological balance. (Zhang et al., 2024; Upton, 2011). These practices both ensure the continuity of the plant in terms of biodiversity and reduce the environmental impact of commercial demand.

Phytochemical components and effects

The therapeutic efficacy of *C. racemosa* is based specifically on the components present in the rhizome and roots of the plant. The most notable of these components is the high content of triterpene glycosides. The main ones are structures such as actein, 27-deoxyactein, cimigenol, cimiracemosides A and B (Zhang et al., 2024). Triterpene glycosides have been implicated in alleviating menopausal symptoms by exhibiting anti-inflammatory, analgesic, and neuroregulatory effects. In addition, phenolic compounds also have an important place in the plant, and hydroxybenzoic acid derivatives such as ferulic acid and isoferulic acid attract attention with their antioxidant properties (Wagner et al., 2011). Isoflavones from the flavonoid class, particularly formononetin, have also been identified, contributing to the herb's hormonal balance-promoting properties with mild estrogen-like effects (Bolzan et al., 2014). In addition, tannins and caffeic acid derivatives are also present in the rhizomes of *C. racemosa*. These compounds are known for their anti-inflammatory and antimicrobial effects (Wilson et al., 2014). The essential oil content of the plant is relatively low and is not considered a major contributor to its pharmacological activity (European Medicines Agency, 2010). Although its alkaloid content is low, these compounds are thought to contribute to the complex pharmacodynamic profile of the plant (Wagner et al., 2011).

Indications and clinical uses

It is known that it has been used for various medicinal purposes for centuries by the indigenous peoples of North America. Its traditional uses include relieving headaches, rheumatism, postpartum uterine contractions, first aid against snakebites, and treating disorders related to the reproductive system in women (Beer et al., 2013; Burdette et al., 2002; Chen et al., 2017). The plant, which has an important place especially in the field of women's health, has also been evaluated as a regulator of uterine tone in the postpartum period (Burdette et al., 2002; Chen et al., 2017).

In modern applications, C. *racemosa* is most commonly used in the management of menopausal symptoms. Its efficacy has been investigated in relation to vasomotor symptoms (hot flashes, night sweats, and sudden bouts of sweating), menopause-related insomnia, anxiety, dysmenorrhea, and premenstrual syndrome (PMS) (Moerman, 1998). In addition, some clinical studies suggest that the plant has positive effects on mood disorders and symptoms of mild depression (Wuttke et al., 2003b). Since the phytoestrogenic effects of *C. racemosa*, which is considered an alternative to hormonal therapies (especially hormone replacement therapy), are based on selective estrogen receptor modulator (SERM)-like mechanisms, it is accepted to offer a safer profile compared to classical estrogen treatments (Wagner et al., 2011). This feature makes its use particularly important in women at risk of breast and endometrial cancer (Burdette et al., 2002; Chen et al., 2017). In evaluations by the European Medicines Agency (EMA) and the World Health Organization (WHO), it has been stated that short-term (usually 3-6 months) use of *C. racemosa* is safe, but it has been emphasized that the current scientific evidence for long-term use is insufficient and more extensive clinical studies are needed (Zhang et al., 2024). Therefore, careful consideration before use is recommended, especially in patients with chronic diseases or a history of hormonal cancers (European Medicines Agency, 2010).

Contraindications and warnings

The use of *C. racemosa* in specific patient groups needs to be carefully evaluated. It is emphasized that the use of this herb is contraindicated due to its phytoestrogenic potential, especially in individuals

with a history of estrogen-sensitive malignancies (e.g., breast cancer, endometrial cancer, or ovarian cancer) (National Center for Complementary and Integrative Health, 2024). Although the herb has a SERM-like effect, there is insufficient clinical data to completely rule out possible risks in these patients (Chen et al., 2017). Regarding pregnancy and lactation periods, clinical studies on the safety of *C. racemosa* are very limited. Therefore, its use is not recommended in women during pregnancy and lactation (Huntley & Ernst, 2003). Since the hormonal activity of the plant may have possible adverse effects on the fetus or infant, it should be used with caution (European Medicines Agency, 2010).

While potential hepatotoxic effects on liver function have been reported, this association has not been conclusively proven. Patients with a history of liver disease should consult a healthcare professional before using this herb (Wagner et al., 2011). Case reports and some clinical investigations have reported idiopathic hepatitis and elevation of liver enzymes after the use of *C. racemosa*; however, in most reports, it has been observed that other hepatotoxic agents are used simultaneously (Coon & Ernst, 2004). Still, regular monitoring of liver function tests is recommended during the use of this herb in individuals with liver disease (European Medicines Agency, 2010). In addition, attention should be paid to the interaction potential of *C. racemosa;* especially when used in combination with hormonal therapies, hepatotoxic drugs, or anticoagulants, side effects or changes in drug efficacy may occur (Wagner et al., 2011).

Side effects and safety profile

In general, *C. racemosa* is considered safe for short-term use (between 3-6 months), and there are mild, temporary side effects (Naser et al., 2011a). The most common adverse effects reported in clinical trials included headache, nausea, dizziness, breast tenderness, mild hypotension, and myalgia (Chen et al., 2017). These side effects have generally been observed to regress with dose adjustment or discontinuation of use (Ulrich et al., 2020). However, although rare, idiopathic hepatitis, elevated liver enzymes, and even liver failure associated with the use of *C. racemosa* have been reported in some case reports (Wuttke et al., 2003a, 2003b). The risk of hepatotoxicity is still controversial due to the simultaneous use of other hepatotoxic drugs in most of these cases (Naser et al. 2011a; Teschke et al., 2011). Regular monitoring of liver function tests is recommended, especially in patients with a history of liver disease and in cases of long-term use (European Medicines Agency, 2010). However, it is considered that the toxic dose of *C. racemosa* is quite high, and the risk of serious side effects is low in the general population. Further randomised controlled trials are needed to clarify safety and long-term use (Naser et al., 2011a).

Herb-drug interactions

C. racemosa has the potential to act on hormonal balance due to its phytoestrogenic and other bioactive compounds. This increases the risk of interactions, especially when used together with estrogen-containing drugs (oral contraceptives, hormone replacement therapies) (Wagner et al., 2011). In addition, pharmacodynamic and pharmacokinetic interactions may occur when used together with drugs such as tamoxifen in the SERM group. Therefore, caution should be exercised in combined therapies (Chen et al., 2017). In addition, due to the hepatotoxicity potential of *C. racemosa* and its effects on the liver, adverse effects on liver function can be seen when used together with hepatotoxic drugs. In simultaneous use with antihypertensive drugs, it is recommended that patients with high blood be careful in these combinations, as there may be a risk of excessive decrease in blood pressure due to the hypotensive effect of the plant (European Medicines Agency, 2010).

From a pharmacokinetic point of view, although some of the components contained in *C. racemosa*

are thought to have effects on the cytochrome P450 (CYP450) enzyme system, these effects, and in particular the potential mechanisms of interaction on the CYP3A4 isoenzyme, have not yet been fully clarified (Gonzalez et al., 2018). Therefore, there is a potential for a theoretical interaction with drugs metabolized via CYP3A4, and caution is advised in clinical use. In summary, close follow-up and dose adjustments are recommended in terms of drug-food interactions in patients using *C. racemosa,* especially when used in combination with hormonal therapies, hepatotoxic agents, and antihypertensive drugs (Fritz et al., 2014; Gurley et al., 2005).

MATERIALS AND METHODS

This review was developed through a literature search. It captures the full breadth of scientific evidence on the phytochemistry, pharmacological activities, clinical efficacy, and safety considerations of *C. racemosa*. A multi-stage search procedure was applied to major scientific databases (PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar) to identify peer-reviewed publications released between 2000 and 2024. To minimise publication bias and ensure comprehensive coverage, reference lists of key review papers, authoritative monographs, and regulatory assessments (EMA, WHO, NCCIH) were also examined manually.

The search strategy used a combination of controlled vocabulary and free-text terms, including: "*Cimicifuga racemosa* L.", "*Actaea racemosa* L.", "black cohosh", "triterpene glycosides", "phytochemical profile", "SERM-like activity", "clinical trial", "menopausal symptoms", "premenstrual syndrome", "safety" and "hepatotoxicity".

Studies on *C. racemosa* had to be of a certain quality and scope. They had to focus on the herb itself, either as a whole extract or as specific compounds from its rhizome. Included were studies on how it works, tested in models of cells or whole organisms, as well as clinical trials and observational studies reporting treatment outcomes. Also included were review articles and analytical papers on how to prepare extracts, their safety, and pharmacological characteristics. Excluded were publications assessing multi-herbal formulations, which lacked the detail and scientific quality needed, or were not available in English or Turkish.

For each study, data were collected on population, preparation, dosage, duration, outcomes, and any adverse effects. This was to identify inconsistencies in the extraction and solvent, and their influence on bioactive compounds and pharmacological interpretation. This approach allowed current evidence to be synthesised, as well as the existing literature's methodological heterogeneity to be critically evaluated.

Table 1. Studies on *Cimicifuga racemosa* (L.) Nutt.

Year	Authors	Study Type	Sample/Model	Extract/Component Used	Dose and Duration	Parameters Examined	Conclusions / Findings	Notes / Suggestions
2002	Liske et al.	*In vitro*	Cell culture	Triterpene glycosides	Not reported	Estrogen receptor binding	No direct estrogen receptor binding observed; neuroregulatory effects suggested *in vitro*	SERM-like mechanism
2003a	Wuttke et al.	Clinical study	Patients with premenstrual syndrome (n=90)	Standardized *C. racemosa* root extract	40 mg/day (standardized BNO 1055 extract)	PMS symptoms	Significant improvement in PMS symptom scores compared to baseline; well-tolerated	Clinically supported
2003b	Wuttke et al.	Clinical study	Menopausal women (n=100)	Standardized *C. racemosa* root extract (40% isopropanol)	40 mg/day, 12 weeks	Vasomotor symptoms	Significant reduction in frequency and severity of hot flashes and night sweats over 12 weeks; well-tolerated	Safe and effective
2003	Huntley & Ernst	Systematic review	Randomized controlled clinical trial	Standardized *C. racemosa* root extract	Not reported	Menopausal symptoms	Evidence suggests superior improvement in menopausal symptoms compared to placebo; long-term efficacy data are insufficient	Long-term data inadequacy
2004	Coon & Ernst	Review	Clinical studies	Standardize *C. racemosa* root extract	Not reported	Psychological symptoms	Positive effects observed on anxiety and depressive symptoms in women; evidence from multiple small studies	Supporting data
2006	Mahady	Review	Not reported	Phytochemical analyses	Not reported	Pharmacology, safety	Triterpene glycosides and other compounds exhibit anti-inflammatory and SERM-like effects; clinical safety is generally acceptable	More clinical trials are needed
2007	Green et al.	*In vivo*	Rat models	Standardized *C. racemosa* root extract (58–60% ethanol)	30 mg/kg, 3 weeks	Antioxidative gene expression changes capacity	Significant reduction of free radicals in treated mice; improved antioxidant status	Preclinical support

Year	Authors	Study Type	Sample/Model	Extract/Component Used	Dose and Duration	Parameters Examined	Conclusions / Findings	Notes / Suggestions
2007	Henz et al.	Clinical study	Menopausal women (n=120)	Standardized *C. racemosa* root extract	40 mg/day, 16 weeks	Psychological symptoms	Significant reduction in anxiety and depressive symptoms; treatment was well-tolerated	More clinical trials are needed
2008	Borrelli et al.	Meta-analysis	Menopausal women	Various *C. racemosa* preparations	Not reported	Phytoestrogenic effect, safety	Improvement in menopausal symptoms observed across studies; positive safety profile; long-term data limited	More long-term work is needed
2009	Schmid et al.	*In vitro*	Human breast cancer cell line	Standardized C. racemosa extract	Not reported	Cell proliferation, apoptosis-inflammatory mechanisms	Extract inhibited proliferation and induced apoptosis in breast cancer cells reduction in inflammatory markers	The mechanism is detailed
2009	Amsterdam et al.	Clinical study	Menopausal women (n=80)	Standardized *C. racemosa* root extract	40 mg/day, 10 weeks	Anxiety scores	Significant reduction in anxiety scores compared to baseline; treatment was well-tolerated	Safe to use
2010	Nuntanakorn et al.	Chemical Analysis	Plant extract	Phenolic compounds	Not reported	Antioxidant activity	Extracts demonstrated significant *in vitro* radical scavenging and antioxidant capacity	Phytochemical richness
2011b	Naser et al.	Systematic review	Case reports	*C. racemosa* preparations	Not reported	Hepatic toxicity	Rare hepatotoxic events reported; causality not fully established	Careful use recommendation
2012	Leach et al.	Systematic review	Randomized clinical trials (16 RCTs, 2027 women)	Different C. racemosa preparations	Not reported	Menopausal symptoms	Some studies indicate improvement in menopausal symptoms; however, overall evidence is inconsistent, and heterogeneous	Lack of long-term efficacy and safety data

Year	Authors	Study Type	Sample/Model	Extract/Component Used	Dose and Duration	Parameters Examined	Conclusions / Findings	Notes / Suggestions
2013	Huang et al.	*In vitro*	Neuronal cell line	Active compounds of 75–80% ethanol and 40% isopropanol extracts	Not reported	Cellular damage and inflammation	Extracts reduced oxidative damage and inhibited inflammatory responses in neuronal cells	More work needed
2013	Mohammad-Alizadeh-Charandabi et al.	Clinical study	Menopausal women (n=84)	Standardized *C. racemosa* root extract	8 weeks	Vasomotor, psychological and physical symptoms	Significant reduction in "Greene Climacteric Scale" scores including psychic domain; no serious side effects	Suggest further studies in varied populations
2014	Wilson et al.	*In vitro*	Cell culture	Isoflavones	Not reported	Estrogenic activity	Low estrogenic effects observed; SERM-like mechanism supported	SERM effect supported
2015	Jiang et al.	Clinical study	Menopausal women (n=100)	Standardized *C. racemosa* root extract	40 mg/day, 12 weeks	Sleep quality	Sleep quality scores improved significantly compared to baseline; minimal adverse effects were reported	Side effects are minimal
2015	Martin et al.	*In vitro*	Cell culture	Flavonoids	Not reported	Antioxidant and anti-inflammatory	Extracts demonstrated strong antioxidant and anti-inflammatory effects *in vitro*	Dose-response studies required
2017	Chen et al.	*In vitro*	Cell culture	Isolated triterpenes	Not reported	Estrogenic activity	SERM-like effects observed; modulation of estrogen receptors suggested	The mechanism is detailed

DISCUSSION

Cimicifuga racemosa (L.) Nutt. has gained attention in recent years as a natural treatment for clinical manifestations such as hot flashes, sweating, sleep disorders, and psychological symptoms, especially in menopausal women. Clinical studies on the effectiveness of the herb have shown positive results in relieving menopausal symptoms. These effects are thought to be achieved by the triterpene glycosides and flavonoids present in the plant, which selectively may bind to and modulate estrogen receptors. This mechanism allows the herb to exert estrogenic effects on a target tissue basis without directly increasing endogenous estrogen levels. Furthermore, the anti-inflammatory and antioxidant properties of *C. racemosa* are thought to play a significant role in reducing inflammation associated with menopause, with suppression of inflammatory pathways and neutralization of free radicals contributing to symptom reduction.

The neuroprotective effects of the plant are considered as a supportive element in the management of psychological disorders common in menopause. These effects are explained by different mechanisms, such as the reduction of oxidative stress in nerve cells and the regulation of neurotransmitter systems. From a security point of view; while *C. racemosa* is generally noted to be well-tolerated in short- to medium-term use, adverse effects on liver function have been reported, although rare. For this reason, careful use is recommended, especially in individuals with chronic diseases or taking medications. The herb's pharmacokinetics and interaction potential should be considered, especially in patients receiving hormone therapy.

In some of the preclinical and clinical studies conducted with *C. racemosa*; it noteworthy that not enough information is given about the preparation method of the extracts used and the type of solvent. These studies ignore these differences by using only the term "standardized", which creates significant methodological limitations in terms of data reproducibility and interpretability. In addition, in some systematic reviews and meta-analysis studies, extract/product type and solvent information are not specified, which makes it difficult to base clinical recommendations. Considering that the solvent and method used have a direct effect on the acquisition, stability, effect, and toxicity of bioactive components; such studies are required to clearly report parameters such as extract type, extraction method, and solvent composition.

After all, *C. racemosa* takes its place in clinical practice as a herbal treatment element in menopausal complaints. However, long-term and randomized controlled clinical trials with standardized preparations are required to clarify efficacy and safety data. In this way, both patient safety can be ensured, and the therapeutic potential of the plant can be revealed more clearly.

CONCLUSION

Research on the clinical efficacy and safety profile of *C. racemosa* focuses on relieving vasomotor symptoms, particularly in menopausal women. Double-blind, placebo-controlled randomized clinical trials have demonstrated the herb's positive effects on hot flashes, night sweats, and psychological symptoms. The fact that the plant does not directly bind to estrogen receptors and may exhibit SERM-like modulatory activity is important in explaining the mechanism of its clinical benefits. However, there are some uncertainties about long-term reliability due to the methodological diversity of the studies, dosage differences, and short-term follow-up.

AUTHOR CONTRIBUTION STATEMENT

The conceptualization, methodology, investigation, data curation, visualization, writing – original draft, writing – review & editing (EB), the conceptualization, methodology, writing – review & editing (GEC).

CONFLICT OF INTEREST

All the authors of this article declared no conflict of interest.

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