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ETHNIC HERBAL MEDICINE IN THE TREATMENT OF PREMENSTRUAL SYNDROME: ETIOLOGY, CLINICAL MANIFESTATIONS AND OTHER MEDICAL INTERVENTIONS

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ABSTRACT

Premenstrual syndrome (PMS) is a disorder which affects women of reproductive age, with an estimated global prevalence of around 47%, with 3-8%, significantly affected in daily functioning. GABA conductance and changes in neurosteroid levels, and allopregnanolone, are suspected role in the disorder's etiology. In this paper, we are providing an overview of recent reports on the etiology and recognized therapeutic approaches along with both the Pharmacological and Non-Pharmacological interventions. The treatment of PMS is crucial for enhancing the quality of life for affected women. Medications used in PMS treatment should be individually selected to achieve the best therapeutic effect, considering the clinical situation of the patients.

Keywords: Premenstrual Syndrome, Estrogen, Progesterone, Hormonal Imbalance, Pharmacological and Non- Pharmacological treatment

INTRODUCTION

During the luteal phase of the menstrual cycle, premenstrual syndrome (PMS) includes clinically significant physical and psychological symptoms that cause

significant distress and functional impairment. After menstruation begins, these symptoms go away in a few days **[1]**. Although 75–80% of women experience mild premenstrual symptoms, only a small percentage report symptoms severe enough to interfere with day-to-day functioning **[2]**. Changes in hunger, weight gain, headaches, back and low back pain, nausea, constipation, anxiety, irritability, rage, exhaustion, restlessness, mood swings, and crying are all signs of premenstrual syndrome (PMS) Although most of the symptoms are modest, 5–8% have moderate to severe symptoms that are linked to significant distress or impairment of functioning. Clinically significant premenstrual symptoms were referred to as premenstrual syndrome (PMS) or premenstrual tension (PMT) in the earliest medical papers on this topic.2. Premenstrual tension syndrome is listed under the section "Diseases of the Genitourinary Tract" in the WHO International Classification of Diseases (ICD). However, similar to PMS and PMT, this definition lacks clear criteria and does not indicate severity, making it useless for clinical diagnosis, medication labeling, or research **[3]**.

The fifth edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-5) has classified the more severe version of the same as premenstrual dysphoric disorder (PMDD) as a psychiatric disease. To reduce these symptoms, a variety of pharmaceutical and nonpharmacological therapeutic approaches are employed. For moderate symptoms, nonpharmacological therapies are the first line of treatment; for severe symptoms, pharmacological therapy—primarily selective serotonin reuptake inhibitors (SSRIs)—is used **[4]**.

Exercise and physical activity, diet, herbal remedies, cognitive behavioral therapy, social support, getting enough sleep, taking regular hot baths, and vitamin supplements are some of the non- pharmacological treatments used to address moderate symptoms.

Etiology

Premenstrual syndrome has an unclear origin. Hormonal imbalances such as excess estrogen and insufficient progesterone have been suggested as PMS symptoms coincide with the menstrual cycle's hormonal swings. Serotonin is also linked to symptoms as a major contributing component.

The three main hormones that make up estrogen are estrone, estradiol, and estriol; the most powerful of these is estradiol. Women's mood swings are caused by fluctuations in estrogen levels during the luteal phase. According to clinical studies, there is a considerable rise in serotonin precursors during days 7–11 and 17–19 of the menstrual

cycle. This suggests that mood disorders and PMS are closely related due to the control of estrogen and serotonin.

According to the molecular biology studies, the decreased estrogen causes the hypothalamus to release norepinephrine, which triggers a decline in acetylcholine, dopamine, and serotonin that leads to insomnia, fatigue, depression, which are common symptoms of PMDD and PMS **[5]**.

According to an Egyptian study, eating too many sweet foods is positively correlated with PMS. It also demonstrated that there was a substantial correlation between PMS and other factors, like coffee and junk food consumption. It follows that there is a strong correlation between lifestyle factors and PMS and PMDD.

Pathophysiology

Premenstrual syndrome has a complicated, ambiguous, and poorly understood pathogenesis. Progesterone's effects on neurotransmitters such as gamma-aminobutyric acid (GABA), opioids, serotonin, and catecholamine are expected to have an impact on PMS. This condition is also thought to be caused by a preexisting serotonin deficit with increased progesterone sensitivity.

PMS is caused by several causes, including genetics, aberrant hypothalamic-pituitary-adrenal (HPA) axis function, insulin resistance, elevated prolactin levels or sensitivity to the action of prolactin, changes in glucose metabolism, and specific nutritional electrolyte shortages. Stress increases the sympathetic nervous system, which in turn causes menstruation discomfort by intensifying the uterine contraction **[6]**.

Epidemiology

According to epidemiological research, between 80% and 90% of women experience at least one PMS symptom; however, between 2.5% and 3% of women experience the illness to a degree that interferes with their social interactions and activities. The term premenstrual dysphoric disorder (PMDD) refers to this condition **[7]**. PMS primarily affects female college students. This population is thought to have a high prevalence of PMS, which has a negative impact on their quality of life and scholastic achievement. For instance, 33.82% of Chinese university students, 37% of Ethiopian students, 39.9% of Taiwanese university students, 65% of Egyptian university students, 72.1% to 91.8% of Turkish university students, and 79% of Japanese university students have PMS **[8-11]**.

Disparities in young adult females' genetic, nutritional, and lifestyle characteristics as well as different community-adopted premenstrual

and menstrual habits may be the cause of this geographic variation in PMS prevalence **[12-14]**.

Hormones

Only when all other options have been exhausted may hormone therapy be recommended. Depending on various views on the etiology of symptoms, estrogen, progestogen, and androgen have all been recommended and administered. However, daily oral contraceptive pills or progestogens, such as depot medroxy-progesterone acetate 150 mg i.m. every three months, oral medroxyprogesterone acetate 10-30 mg daily, oral medroxyprogesterone acetate 10-3 mg daily, or deyhydrogesterone 20 mg daily, are likely more effective in eliminating endogenous hormone variations. Between 60 and 70 percent of PMS patients have found success with GnRH agonists. There are serious adverse outcomes from this medical oophorectomy. Its combination with oestrogen-progestogen add-back reduces both the negative effects and the effectiveness of PMS treatment.

Other Drugs

Although it has been tried, bromocriptine is most effective at reducing cyclical breast symptoms. The overall benefit is not much higher than what would be achieved with placebo therapy plus a sympathetic doctor, even though some additional symptoms are alleviated or made bearable. Mild tranquilizers are helpful when there is anxiety and emotional instability. While some proprietary medicines contain progestogens, anti-histamine stimulants, and tranquilizers, the majority contain combinations of vitamins and minerals.

SURGERY

In certain severe situations, no drug may be able to provide relief. For these women, HRT with unopposed estrogen has been advised after total abdominal hysterectomy with bilateral salpingo-oophorectomy. To ensure that the treatment would be effective, a test with a GnRH analogue should be conducted, nevertheless, as this is an extreme step. Sufficient counseling is necessary **[15]**.

Clinical presentation

Physical, emotional, and behavioral symptoms are all present in PMS.

1. Manifestations

- Bloating
- Tenderness of the breasts
- Weariness
- Headaches **[16]**

2. Symptoms of Emotion

- The ability to irritate
- Fear
- Depression
- Mood fluctuations **[17]**

3. Signs of Behavior

- Cravings for food
- Disturbances in sleep
- Diminished focus **[18]**

DIAGNOSIS

The diagnosis depends on the cyclic nature of the symptoms, which are limited to the luteal phase and go away following menstruation.

The American College of Obstetricians and Gynecologists' (ACOG) criteria, which comprise the following, serve as the basis for diagnosis:

1. Only the luteal phase symptoms.
2. The follicular phase's symptomless periods.
3. A notable hindrance to day-to-day activities.

A journal of symptoms during two menstrual cycles helps with diagnosis **[19]**.

Premenstrual syndrome can be a symptom of a number of clinical conditions. Psychiatric disorders such as substance abuse disorders, affective disorders (such as depression, anxiety, dysthymia, and panic), gynecological disorders like endometriosis and dysmenorrhea, medical conditions like hypothyroidism, perimenopause, and anemia are among them. Therefore, it is crucial to obtain a thorough medical history, conduct a thorough physical examination, and rule out these illnesses **[20]**.

Modifications

1. Lifestyle modifications

The first step to managing PMS is to lead a healthy lifestyle. Lifestyle changes are frequently sufficient for many women to manage their symptoms. Here is an example of advice on changing one's lifestyle.

(i) To lessen bloating, fluid retention, and other symptoms, drink lots of water or juice instead of soft drinks, alcohol, or other caffeinated beverages.

(ii) Avoid overeating, eat small meals frequently, and wait no more than three hours between snacks.

(iii) Consume a well-balanced diet that includes more fruits, vegetables, and whole grains and little to no sugar and salt.

(iv) A medical professional might suggest dietary supplements such as calcium, magnesium, and vitamin B6.

(v) To assist lessen the intensity of PMS symptoms; engage in regular aerobic exercise throughout the month **[21]**.

2. Pharmacological interventions

(i) For severe PMS/PMDD, selective serotonin reuptake inhibitors (SSRIs) are the first line of treatment **[22]**

(ii) Hormonal Therapies: Contraceptives used orally help to balance out variations in hormones **[23]**.

(iii) NSAIDs: Reduce physical discomfort and agony **[24]**.

(i) Vitamin B6 and calcium are useful in lowering emotional and physical problems **[25]**.

(ii) Chaste berry Extract: Shows promise in reducing symptoms, but further research is required **[18]**.

4. The goal of cognitive-behavioral therapy (CBT) is to address disruptive, unresolved ideas, actions, and emotions. CBT assists in identifying these habits and in creating coping mechanisms to enhance day-to-day functioning **[26]**.

5. The only herbal remedy that has been shown to manage the mood swings and irritation linked to PMS is the fruit extract Vitex agnus-castus **[27]**.

Ethnic Herbal Medicine Used for Premenstrual Syndrome

PMS is defined as a condition with emotional, physical, and behavioural symptoms that increase in severity during the luteal phase of the menstrual cycle and resolve by the end of menstruation. By definition, there must be a symptom-free interval after menstruation and before ovulation. Generally, symptoms are observed up to 14 days before the start of menses, causing impairment of life, with anger and irritability being the most severe and long lasting symptoms. The exact cause of PMS is unknown **[28]**. However, studies have shown that 3–8% of menstruating women are affected by PMS and that 15–20% of women meets the criteria for subclinical PMS **[29]**. A review reported incidences of PMS globally are 40, 85, 46, and 60% for Europe, Africa, Asia, and South America, respectively **[30]**.

The management of PMS is generally performed in a step-wise manner from non-pharmacological strategies, antidepressant medications, and hormonal strategies, with surgical options being considered as a last resort **[31]**. Studies have shown a more sustained but less rapid improvement with the use of selective serotonin reuptake inhibitors (SSRIs). Vitamin B6 is also well-known as the first-line treatment for PMS **[32]**. However, peripheral neuropathy of pyridoxine is characterized at doses greater than 200 mg/day **[33]**. Therefore, herbs with lower costs, better benefits, and lesser side effects have become complementary and alternative treatments for women to improve PMS.

As a concept, PMS was put forward by western medicine doctors 70 years ago, and only a handful of herbal medicines are recorded in Western countries for the treatment. In Western countries, anti-depressive drugs, hormonal treatment, and analgesics dominate the treatment of PMS; and plant extracts such as *Vitex agnus-castus* L. is commonly considered as an

alternative therapy in English-speaking countries **[34]**.

In China, the use of Chinese herbal medicine (CHM) is very common in the treatment of PMS. Liver qi stagnation and Yin Blood deficiency are proposed as the most common root causes of PMS, and the fundamental treatment principles for PMS involve measures to regulate Liver qi to resolve stagnation and tone blood **[35]**.

The most common medicines for the relief of PMS are Chaihu (*Bupleurum chinense* DC.), Xiangfu (*Cyperus rotundus* L.), Danggui (*Angelica sinensis* (Oliv.) Diels), Baishao (*Paeonia lactiflora* Pall.), and formulas such as Xiaoyao Powder and Jiawei Xiaoyao Powder (JXP). In Taiwan, JXP-centered CHM combinations were most commonly prescribed for PMS. The top 10 most commonly used single herbs for PMS are *Cyperus rotundus* L., *Leonurus japonicus* Houtt.(Oriental motherwort), *Cory dalis yanhusuo* (Y. H. Chou and Chun C. Hsu) W. T. Wang ex Z. Y. Su and C. Y. Wu, *Salvia miltiorrhiza* Bge., *Eucommia ulmoides* Oliv., *Scutellaria baicalensis* Georgi, *Dipsacus asperoides* C. Y. Cheng at T. M. Ai, *Cuscuta chinensis* Lam. or *Cuscuta japonica* Choisy, *Pueraria lobata* (Willd.) Ohwi, *Paeonia* × *suffruticosa* Andrews. The top five most commonly used herbal formulas for the treatment of PMS are JXP, Danggui Shaoyao Powder, Guizhi Fuling Pills, Wenjing Decoction, and Shaofu Zhuyu Decoction [36]. The ingredients of these Chinese herbal formulas are listed in **Table 1**.

Table 1: The ingredients of the Chinese Herbal Formulas

Name	Number of ingredients	Ingredients	References
Danggui Shaoyao Powder	**6**	**Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), Chuanxiong Rhizoma (*Ligusticum chuanxiong* Hort.), Alismatis Rhizoma (*Alisma orientate* (Sam.) Juzep), Angelicae Sinensis Radix (*Angelica sinensis* (Oliv.) Diels), Poria (*Poria cocos* (Schw.) Wolf), and Atractylodis Rhizoma alba. (*Atractylodes macrocephala* Koidz.)**	**Lee HW *et al.* (2016) [37]**
Guizhi Fuling Pills	**5**	***Cinnamomi Cortex (Cinnamomum cassia Presl)*, Poria (*Poria cocos* (Schw.) Wolf), Moutan Cortex (*Paeonia suffruticosa* Andr.), Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), and Persicae Semen (*Prunus persica* (L.) Batsch)**	**Sun *et al.* (2016) [38]**
GeGen Decoction	**7**	**Puerariae Lobatae Radix (*Pueraria lobata* (Willd.)Ohwi), Ephedrae Herba (*Ephedra sinica* Stapf), Cinnamomi Cortex (*Cinnamomum cassia* Presl), Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), Glycyrrhizae Radix Et Rhizoma (*Glycyrrhiza uralensis* Fisch.), Rhizoma Zingiberis recens (*Zingiber officinale* Roscoe) and Jujubae Fructus (*Ziziphus jujuba* Mil.)**	**Chai *et al.* (2020) [39]**
Jiawei Xiaoyao Powder	**9**	**Bupleuri Radix (*Bupleurum chinense* DC.), Angelicae Sinensis Radix (*Angelica sinensis* (Oliv.) Diels), Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), Atractylodis Rhizoma (*Atractylodes macrocephala* Koidz.), Smilacis Glabrae Rhizoma (*Smilax glabra* Roxb.), Glycyrrhizae Radix Et Rhizoma (*Glycyrrhiza uralensis* Fisch.), Moutan Cortex (*Paeonia suffruticosa* Andr.), Gardeniae Fructus (*Gardenia jasminoides* Ellis), Menthae Haplocalycis Herba (*Mentha canadensis* L.)**	**Li *et al.* (2019) [40]**
Shaofu Zhuyu Decoction	**10**	**Foeniculi Fructus (*Foeniculum vulgare* Mill.), Rhizoma Zingiberis recens (*Zingiber officinale* Roscoe), Cinnamomi Cortex (*Cinnamomum cassia* Presl), Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), Angelicae Sinensis Radix (*Angelica sinensis* (Oliv.) Diels),**	**Lee H *et al.* (2016) [41]**

		Chuanxiong Rhizoma (*Ligusticum chuanxiong* Hort.), Myrrh (*Commiphora myrrha* Engl.), Corydalis Rhizoma (*Corydalis yanhusuo* W. T. Wang), Typhae Pollen (*Typha angustifolia* L.), and Faeces Trogopterpri (*Trogopterus xanthipes* Milne Edwards)	
Wenjing Decoction	**12**	**Asini Corii Colla (*Equus asinus* L.), Ophiopogonis Radix (*Ophiopogon japonicus* (L. f) Ker-Gawl.), Pinelliae Rhizoma (*Pineilia ternata* (Thunb.) Breit.), Angelicae Sinensis Radix (*Angelica sinensis* (Oliv.) Diels), Glycyrrhizae Radix Et Rhizoma (*Glycyrrhiza uralensis* Fisch.), Cinnamomi Cortex (*Cinnamomum cassia* Presl), Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), Chuanxiong Rhizoma (*Ligusticum chuanxiong* Hort.), Ginseng Radix Et Rhizoma (*Panax ginseng* C. A. Mey), Moutan Cortex (*Paeonia suffruticosa* Andr.), Euodiae Fructus (*Euodia rutaecarpa* (Juss.) Benth.) and Rhizoma Zingiberis recens (*Zingiber officinale* Roscoe)**	**Gao *et al.* (2017) [42]**
Xiaoyao Powder	**8**	**Bupleuri Radix (*Bupleurum chinense* DC.), Radix Angelicae Sinensis Radix (*ASngelica sinensis* (Oliv.) Diels), Paeoniae Radix Alba (*Paeonia lactiflora* Pall.), Atractylodis Rhizoma (*Atractylodes macrocephala* Koidz.), Poria (*Poria cocos* (Schw.) Wolf), Glycyrrhizae Radix Et Rhizoma (*Glycyrrhiza uralensis* Fisch.), Menthae Haplocalycis Herba (*Mentha canadensis* L.), and Rhizoma Zingiberis recens (*Zingiber officinale* Roscoe)**	**Liu *et al.* (2021) [43]**

In Iran, *Salvia officinalis* L. extract appears to be more effective in reducing the physical and psychological symptoms associated with PMS, when compared to placebo **[44]**. In Persian traditional medicine, saffron (dried stigma of *Crocus sativus* L.) is used for depression, which has been confirmed by modern medicine to be achieved through a serotonergic mechanism **[45]**.

A review about treatments in Iran has shown a reduction in PMS symptoms after consumption *Hypericum perforatum* L. (St. John's wort), *Vitex agnus-castus* L. (Chasteberry), *Crocus sativus* L. (saffron), *Ginkgo biloba* L. (ginkgo), and soy **[46]**. This is consistent with the data that we collected.

In Japan, Kampo medicine is the most preferred treatment choice for PMS. Kampo is a part of the official Japanese medical system and it is used alone or in combination with Western medicine for the treatment of complex health conditions, such as chronic health problems, age-related health problems, and lifestyle or stress-related disorders. We recorded 22 types of kampo's that are the most commonly used ingredients (single herb) in PMS **[47]** as shown in **Table 2**.

Inochinohaha White is considered a medicine primarily used to treat PMS by attenuating anxiety-like behavior through GABAA receptor and brain-derived neurotrophic factor expression, which composed of 11 herbs: *Angelica sinensis* (Oliv.) Diels, *Paeonia lactiflora* Pall., *Atractylodes lancea* (Thunb.) DC., *Cinnamomum verum* J. Presl, *Rheum palmatum* L., *Panax ginseng* C. A. Meyer, *Cnidium monnieri* (L.) Cusson, *Poria cocos* (Schw.) Wolf, *Alisma plantago-aquatica* L., *Paeonia suffruticosa* Andr. and *Prunus persica* (L.) Batsch **[48]**.

Table 2: Japanese Herbal Medicine for Treating Premenstrual Syndrome

Family	Scientific name	Used Part	Habit
Lauraceae	*Cinnamomum cassia* (L.) J. Presl	Bark	Tree
Paeoniaceae	*Paeonia lactiflora* Pall.	Root	Herb
Rosaceae	*Prunus persica* (L.) Batsch	Seed	Tree
Paeoniaceae	*Paeonia* × *suffruticosa* Andrews	Bark	Shrub
Asteraceae/Compositae	*Atractylodes lancea* (Thunb.) DC.	Rhizome	Herb
Alismataceae	*Alisma orientalis* (Sam.) Juzep.	Rhizome	Herb
Polyporaceae	*Poria cocos* (Schw.) Wolf	Root	
Apiaceae	*Ligusticum chuanxiong* Hort.	Rhizome	Herb
Apiaceae	*Angelica acutiloba* var. *linearilobа* (Kitag.) Hikino	Root	Herb
Papaveraceae	*Corydalis yanhusuo* (Y. H. Chou and Chun C. Hsu) W. T. Wang ex Z. Y. Su and C. Y. Wu	Tuber	Herb
Ostreidae	*Ostrea gigas* thunberg	Root	
Fabaceae	*Glycyrrhiza uralensis* Fisch.	Root	Herb
Zingiberaceae	*Amomum villosum* var. *xanthioides* (Wall. ex Baker) T. L. Wu and S. J. Chen	Semen	Herb
Araliaceae	*Panax ginseng* C. A. Meyer	Root	Herb
Araceae	*Pinellia ternate* (Thunb.) Breit	Tuber	Herb
Rutaceae	*Aurantii Nobilis* Pericarpium	Peel	Tree
Zingiberaceae	*Zingiber officinale* Roscoe	Rhizome	Herb
Polyporaceae	*Polyporus umbellatus*		
Apiaceae	*Foeniculum vulgare* Mill.	Seed	Herb
Zingiberaceae	*Alpinia officinarum* Hance	Rhizome	Herb
Rhamniaceae	*Ziziphus jujuba* Mill.	Fruit	Tree

In Korea, herbal medicines for the treatment of PMS are *Hypericum perforatum* L. (St. John's Wort), Odor of *Crocus sativus* L. (saffron), *Vitex agnus-castus* L. (Chasteberry), *Ginkgo biloba* L. (Ginkgo), *Cirsium japonicum* (Thunb.) Fisch. ex DC. (Cirsii Japonici Herba Carbonisata), *Elsholtzia splendens* Nakai ex F. Maekawa **[49]**.

In South Africa, the pharmaceutical application of valerian (*Valeriana officinalis* L.) for the treatment of PMS is due to its sedative, anticonvulsant, hypnotic effects, and anxiolytic activity **[50]**.

Prognosis

With the exception of oophorectomy and menopause, PMS symptoms can typically return after quitting medication **[51]**.

Complications

If left untreated, PMS can have an impact on one's sexual life and increase sexual distress, which can lead to marital troubles and other psychological disorders **[52]**. Additionally, there is evidence linking PMS to a higher risk of suicide in women who are hormone sensitive **[53]**.

Deterrence and Patient Education

A prevalent issue among women of reproductive age is premenstrual syndrome. Discussing the issue with the patient who has empathic hearing and offering insight into the causes of her issues is known as patient

education. The patient benefits from the partner's comprehension of the issue when they seek therapy from the healthcare practitioner or at home.

Reproductive health education benefits the patient-physician connection, which facilitates the expression of symptoms and the pursuit of therapy. Teaching family members and significant others supportive actions that lessen PMS symptoms is equally vital. CBT therapies that are couple based have a significant effect on behavioral coping and produce superior results. Due to its prevalence, widespread education about PMS diagnosis and efficient treatment via radio, television, or digital media is also highly beneficial **[54]**.

Evaluation

A number of different physical and mental illnesses must be ruled out in order to diagnose PMS and PMDD. The diagnosis is supported by three factors:

(1) Symptoms that is consistent with PMS;

(2) Symptoms that should only occur during the luteal phase of the menstrual cycle; and

(3) Adverse effects on the patient's function and way of life. Patients should be encouraged to record their premenstrual symptoms in a journal for several months in order to check for cycle-to-cycle fluctuation once the doctor has serious doubts about the diagnosis **[55]**.

Follicle-stimulating hormone (FSH), estradiol (E2), thyroid-stimulating hormone (TSH), prolactin, and cortisol should be ordered as part of the first workup for diagnosis, which may also involve ruling out other pathologies such as hyperprolactinemia, Cushing syndrome, and thyroid abnormalities **[56]**.

CONCLUSION

To identify potentially related factors, more focused epidemiological research is warranted. However, noticing the fact of significant prevalence and its potential impact on the population, stakeholders and policymakers need to address this problem at the community and individual level.

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