

Natural compound for the treatment of Rheumatoid arthritis (RA)-A Review

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ABSTRACT

Turmeric, particularly its components like curcumin and essential oils, has demonstrated potential anti-inflammatory properties relevant to rheumatoid arthritis (RA). Research indicates that these compounds can modulate inflammatory pathways, potentially reducing joint pain, swelling, and stiffness associated with RA. While curcumin has been more extensively studied, turmeric oil also contains constituents that contribute to anti-inflammatory effects. Studies have shown that components found in the essential oils of turmeric, have shown anti-arthritis effects in animal models. However, it is important to note that the bioavailability of the active compounds can be low, and more clinical trials are needed to fully establish the efficacy of turmeric oil and its components for RA. Therefore, while promising, turmeric should be considered a complementary therapy and not a replacement for conventional RA treatment.

Keywords: Turmeric oil, Anti-inflammatory, Rheumatoid arthritis Curcuma longa, Inflammation, Antioxidant, Autoimmune disorder.

I. INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disorder in which a person's immune system attacks the lining of the joints in the body. In a healthy person, the immune system fights with invaders, such as bacteria and viruses. With an autoimmune disease like RA, the immune system mistakes the body's cells for foreign particles and releases inflammatory chemicals that attack those cells. which in severe cases can lead to permanent damage to the joints and disability. Also, RA can involve other organs, including the lungs, heart, blood vessels, skin and eyes [1]. Rheumatoid arthritis (RA) is a T-cell mediated chronic inflammatory disorder with an occurrence of 0.5–1% . 3:1 female are affected in most populations by rheumatoid arthritis.[2] The symptoms include joint stiffness, fatigue, fever, tender, swollen joint.

The risk factors of rheumatoid arthritis include age, gender, smoking, obesity, family history etc.

1.1 Pathophysiology of rheumatoid arthritis: Rheumatoid arthritis (RA) is one of the most common systemic diseases, it is a chronic inflammatory joint disease, and it has been the subject of study as an autoimmune disorder prototype for a long time. Yet, the causes of RA remain to be unknown. Abnormalities in various immunological systems, inflammatory pathways, gene-gene interactions, as well as disturbances in metabolic pathways, are the major factors in the development of RA.[3]

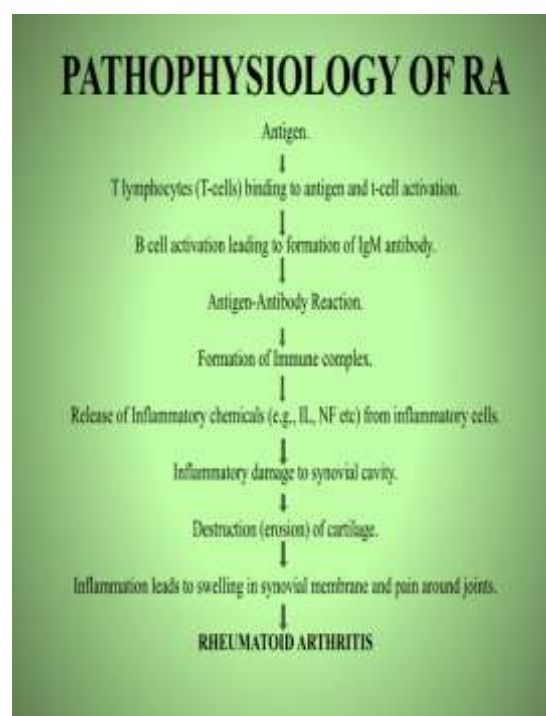


Fig.1 Representation of pathophysiology of RA

Etiology: Doctors don't know exactly what causes this disease. But they know these things could be risk factors for RA.

Age	RA can affect you at any age, but it is most common between 40 and 60.
Gender	Women are more likely than men to develop rheumatoid arthritis.
Family History	If someone in your family has it, you may be more likely to get it.
Environment	A toxic chemical or infection in your environment can up your odds.
Excess Weight	people who are overweight appear to be at a somewhat higher risk of developing rheumatoid arthritis
Smoking	Cigarette smoking increases your risk of developing rheumatoid arthritis, particularly if you have a genetic predisposition for developing the disease.[4]

Table.1 Represent risk factor of RA

1.3 Symptoms of rheumatoid arthritis:

1. Pain, swelling, stiffness and tenderness in more than one joint.
2. Stiffness, especially in the morning or after sitting for long periods.
3. Pain and stiffness in the same joints on both sides of your body.
4. Fatigue and weakness. [5]

1.4 Complications: Rheumatoid arthritis (RA) is a chronic inflammatory disorder that can affect more than just your joints. Here are some complications that can arise from RA:

1. **Joint Damage:** Progressive inflammation can destroy the cartilage and bone around affected joints, leading to deformities and immobility.
2. **Osteoporosis:** RA increases the risk of osteoporosis; a condition that weakens bones and makes them more prone to fractures.
3. **Cardiovascular Disease:** People with RA are at a higher risk of developing cardiovascular diseases, such as heart attacks and strokes.
4. **Lung Disease:** Inflammation can affect the lungs, leading to conditions like pleurisy and pulmonary fibrosis.
5. **Eye Problems:** RA can cause inflammation in the eyes, leading to conditions like scleritis and Sjögren's syndrome.
6. **Anaemia:** Chronic inflammation can lead to a decrease in red blood cell production, causing anaemia. [6]



Fig.2 Representation of RA symptoms

1.5 Treatment of rheumatoid arthritis:

In many research there is no proper cure of rheumatoid arthritis, but different types of treatment is available in pharmaceutical industry allopathic as well as ayurvedic.

Ayurvedic treatment of rheumatoid arthritis: Research has indicated that ayurveda therapy for arthritis, such as herbal preparations and panchakarma therapy can benefit patient with rheumatoid arthritis and enhance the quality of life.[7]

Homoeopathy treatment of rheumatoid arthritis:

Rheumatoid arthritis can be effectively treated with homeopathy with no side effects at all because homeopathic medicines are of natural origin and free of any toxins. It can reduce the severity and frequency of your pain significantly, enhance your range of motion, and avoid any deformity of joints[8]

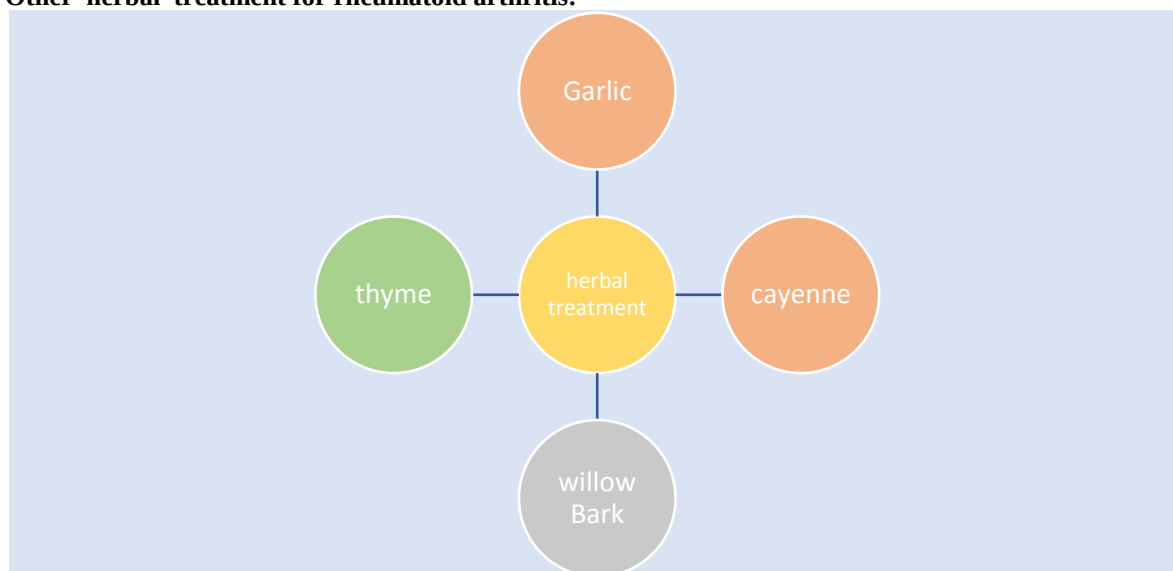
Allopathic treatment of rheumatoid arthritis:

Low doses of nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for pain relief. At

prescription levels, they are also useful in controlling inflammation.[9]

DMARDs. Traditional synthetic disease modifying antirheumatic drugs (DMARDs), most often methotrexate, are sometimes the first medicine you will take to reduce the activity of disease in RA. Other DMARDs that treat RA are leflunomide, sulfasalazine and hydroxychloroquine. Occasionally two or more DMARDs are used in combination.

Other herbal treatment for rheumatoid arthritis:



1. Thyme: It's been found to have anti-inflammatory and antimicrobial properties that
2. Garlic: it helps in ease rheumatoid arthritis.
3. Black pepper: pipeline administration relieved inflammation, pain, could be therapeutic for rheumatoid arthritis.
4. Cinnamon: Cinnamon supplementation may enhance the reduction of inflammation and oxidative stress levels in human and other symptoms of arthritis .
5. Cayenne: Cayenne and other chilli peppers contain capsaicinoids, which are natural compound that have anti-inflammatory properties.
6. Willow Bark: it has significant anti-inflammatory properties and reduce various markers of inflammation.
7. Indian Frankincense: it is found in India and north Africa; Indian frankincense have strong anti-inflammatory properties.

8. Thunder God Vine: Traditional Chinese medicine reduce inflammation from autoimmune disease.
9. Ashwagandha: eases pain and joint swelling in people with rheumatoid arthritis.
10. Ginger: they include the ability to suppress inflammatory molecules called leukotrienes. [10]

1.6 What is turmeric: Turmeric is a spice which has been used as a natural and traditional healing remedy in Ayurvedic medicine for thousands of years. It is a powerful antioxidant and anti-inflammatory that helps prevent blood clots. It is also delicious, and I use it almost daily in my food preparation. Turmeric adds a deep yellow, almost orange colour to your food, and has a unique, mild flavour.

Turmeric (*curcuma longa*) is a rhizome, and the fresh turmeric looks a little like a ginger rhizome. It is a deep orange colour, and stains when you cut it or touch it. Try to get it as a raw

rhizome because it is the most potent in that fresh form.

Fresh turmeric rhizomes are often available at Indian or Asian stores. If fresh turmeric is not available, turmeric powder is a cheap substitute. Health food or Asian stores are the places to buy the powder. Do not buy capsules, they have often been processed and have harmful additives. [11]



Fig. 3 Representation of Turmeric Plant



Fig.4 Representation of local Turmeric

1.7 Turmeric as a remedy:List of ailments where turmeric has successfully been used as a cure.

Turmeric	Used as Anti-inflammatory
Turmeric	Used as Antioxidant
Turmeric	Used as Antidiabetic
Turmeric	Used as Antimicrobial

Table.2 Represent turmeric uses.

- Diabetes - blood sugar normalisation, treats insulin resistance.

- Inflammation. Turmeric prevents inflammation by affecting many pathways that cause inflammation, because it is an adaptogen, an antioxidant, helps stabilise and normalise hormones, and has no side effects except being soothing. [12]
- Detoxification, liver function, gallbladder and production of bile salts.
- Excessive turmeric consumption can lead to constipation (so drink plenty of water), accelerated heartbeat, and excessive blood thinning.[13]

1.8 Turmeric vs curcumin: When reading about turmeric, you will often see curcumin mentioned in the same line. While turmeric is the spice made of the roots of *Curcuma longa*, curcumin is the main active compound of interest also known as a “curcuminoid” within turmeric.[14]

Cultivation:Turmeric can be cultivated in diverse tropical conditions, up to 1,600 meters from the sea level, with temperatures varying from 20-40°C, and rainfall above 1500mm. It is a nine-month crop sown in July and harvested in April. Turmeric thrives in well drained, fertile, sandy and black, red or alluvial loams, rich in humus and uniform in texture. Rich loamy soils having natural drainage and irrigation facilities are the best. Turmeric cannot stand water stagnation or alkalinity.[15]

Harvesting and Curing

The crops are ready for harvest in seven to nine months depending on the time of sowing. The harvest is carried out during January to March. It matures in about 9 months.

The marketing season is from February to May. The leaves of crop turn dry and are light brown and yellowish in colour on maturity, height of crop around 1.5 feet after the complete growth with maximum 8-10 branches with cracks development on soil signifies good yields of turmeric.

The land is ploughed and the rhizomes are carefully lifted with a spade. Harvested rhizomes are cleaned of mud and other extraneous matter adhering to them. The green rhizomes are boiled in water, which are spread out on a clean floor and allowed to dry in the sun for about 15-20 days. They are stirred 3-4 times to ensure uniform drying.

The rounds and figures are dried separately. The former takes more time to dry. When fully dried, turmeric becomes hard and stiff. The dried turmeric is rubbed against the hard surface of the drying floor or templed under feet

covered with piece of gunny cloth and the scales and the root bases are separately by winnowing. Rhizomes for seed are generally heaped in the shade of these or in well-ventilated sheds and covered with turmeric leaves.[16]

1.9 What are the chemical constituent of turmeric ?

Turmeric (*Curcuma longa*) is a plant with a rich composition of bioactive compounds. Its primary chemical constituents include:

Curcuminoids: These are phenolic compounds responsible for turmeric's vibrant yellow colour and many of its health benefits. The main curcuminoids are:

- Curcumin (the most abundant and studied compound)
- Desmethoxycurcumin
- Bisdemethoxycurcumin

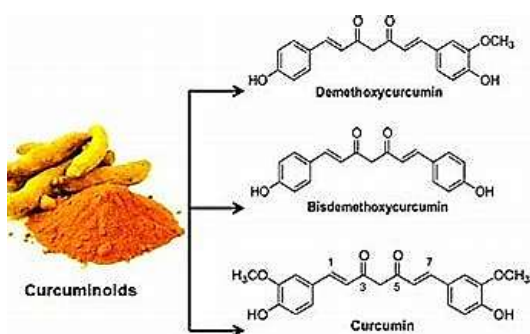


Fig.5

Representation of chemical structure

Essential Oils: These contribute to its aroma and potential therapeutic properties. Key components include: AR-turmerone, Alpha-turmerone, Beta-turmerone, Cineole, Zingiberene.[17]



Fig.6 Represent structure of essential oil.

1.10 Classification:

Kingdom	Plantae
Division	Magnoliophyta
Class	Liopsida
Sub class	Zingiberidae
Order	Zingiberales
Family	Zingiberaceae
Genus	Curcuma
Species	Longa

Table.3 classification of turmeric.

1.11History: *Curcuma longa* has been cultivated for thousands of years in India and Southeast Asia. The plant was introduced to China and Africa in the 7th and 8th centuries. In recounting his travels, *Curcuma longa* was eventually introduced to Jamaica in the 18th century. Currently, commercial production is primarily focused in India and Southeast Asia. The plant is cultivated in home gardens in tropical areas throughout the world. Indigenous systems of medicine, including the Chinese and Ayurvedic systems, have widely used turmeric for centuries in the treatment of many inflammatory conditions and diseases. In India, turmeric has been traditionally used primarily for arthritic and muscular disorders, while in China it has been used as a topical analgesic and for conditions ranging from flatulence, colic, and ringworm to hepatitis and chest pain(18).

1.12Morphology of *Curcuma longa*:

Curcuma longa is a perennial herb, with a short stem, tufted leaf and the rhizomes, which are short and thick and from root to leaves about 2 feet long, deeply veined leaves that project upward from stems that grow from the base of the plant. The leaf colour is deep green and the surface is glossy and smooth. The flowers range from white to light yellow and form a tall spike. The rhizomes, specialized underground stems that are root-like in structure have a brown surface and bright orange or yellow interior flesh and after cutting, it is in curved cylindrical or oblong tubers 2 or 3 inches in length, and an inch in diameter, pointed or tapering at one end, yellowish externally, with transverse, parallel rings internally deep orange or reddish

brown, marked with shining points, dense, solid, short, granular fracture, forming a lemon yellow powder.[19]



Fig.7 Showing roots and leaf of turmeric.

1.13 Pharmacological action of curcuma longa:

Antioxidant Effects: Free radicals can originate from environmental chemicals, tissue injury, infections and auto-immune processes. Antioxidants protect the body from damage from free radicals. Water- and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. One study showed curcumin to be eight times more powerful than vitamin E in preventing lipid peroxidation. A study of ischemia in the feline heart demonstrated that curcumin pretreatment decreased ischemia-induced changes in the heart. An in vitro study measuring the effect of curcumin on endothelial heme oxygenase-1, an inducible stress protein, was conducted utilizing bovine aortic endothelial cells. Incubation (18 hours) with curcumin resulted in enhanced cellular resistance to oxidative damage.

Hepatoprotective Effects: Turmeric has been found to have a hepatoprotective characteristic similar to silymarin. Animal studies have demonstrated turmeric's hepatoprotective effects from a variety of hepatotoxic insults, including carbon tetrachloride (CCL), galactosamine, acetaminophen (paracetamol) and Aspergillus aflatoxin. Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of pro inflammatory cytokines. In rats with CCl-induced acute and subacute liver injury, curcumin administration significantly decreased liver injury in test animals compared to controls. Turmeric and curcumin also reversed biliary hyperplasia, fatty changes, and necrosis induced by

aflatoxin production. Sodium curcumin ate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin, as well as increasing bile solubility, therefore possibly preventing and treating cholelithiasis.

Anti-inflammatory Activity: The volatile oils and curcumin of *Curcuma longa* exhibit potent anti-inflammatory effects. Oral administration of curcumin in instances of acute inflammation was found to be as effective as cortisone or phenylbutazone, and one-half as effective in cases of chronic inflammation. In rats with Freund's adjuvant-induced arthritis, oral administration of *Curcuma longa* significantly reduced inflammatory swelling compared to controls. In monkeys, curcumin inhibited neutrophil aggregation associated with inflammation. *Curcuma longa*'s anti-inflammatory properties may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and neutrophil function during inflammatory states. Curcumin may also be applied topically to counteract inflammation and irritation associated with inflammatory skin conditions and allergies. After intraperitoneal administration, curcumin and sodium curcumin ate exhibited strong anti-inflammatory activity in the carrageenin-induced oedema test in rats and mice.

Anticarcinogenic Effects:- Animal studies involving rats and mice, as well as in vitro studies utilizing human cell lines, have demonstrated curcumin's ability to inhibit carcinogenesis at three stages: tumour promotion, angiogenesis, and tumour growth. In two studies of colon and prostate cancer, curcumin inhibited cell proliferation and tumour growth. Turmeric and curcumin are also capable of suppressing the activity of several common mutagens and carcinogens in a variety of cell types in both in vitro and in vivo studies. The anticarcinogenic effects of turmeric and curcumin are due to direct antioxidant and free-radical scavenging effects, as well as their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens, and inhibiting nitrosamine formation[20]

Antimicrobial Effects: Extract and the essential oil of *Curcuma longa* inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi. A study of chicks infected with the phytochemical and comparative study of Tulsi and turmeric for antimicrobial activity caecal parasite *Eimeria maxima* demonstrated that diets supplemented with 1-

percent turmeric resulted in a reduction in small intestinal lesion scores and improved weight gain. Another animal study, in which guinea pigs were infected with either dermatophytes, pathogenic Molds or yeast, found that topically applied turmeric oil inhibit dermatophytes and pathogenic fungi. but neither curcumin nor turmeric oil affected the yeast isolates Improvements in lesions were observed in the dermatophyte- and fungi-infected guinea pigs, and at seven days post-turmeric application the lesion's disappeared Curcumin has also been found to have moderate activity against Plasmodium falciparum and Leishmania major organisms[21]

Cardiovascular Effects: Turmeric's protective effects on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low-density Lipoprotein (LDL) to lipid peroxidation and inhibiting platelet aggregation. These effects have been noted even with low doses of turmeric. A study of 18 atherosclerotic rabbits given low-dose (1.6-3.2 mg/kg body weight, daily) turmeric extract demonstrated decreased susceptibility of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. The higher dose did not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases were noted, although to a lesser degree than with the lower dose. Turmeric extract's effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines and increased conversion of cholesterol to bile acids in the liver Inhibition of platelet aggregation by Curcuma longa constituents is thought to be via potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis.[22]

Gastrointestinal Effects:- Extract of Curcuma longa exert several protective effects on the gastrointestinal tract. Sodium curcumin ate inhibited intestinal spasm and p-polymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been shown to inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine, significantly increasing gastric wall mucus in rats[23]

Dosage: A dose of turmeric powder is 500-8,000 mg per day used in human studies. Standardized extracts are typically used in lower amounts, in the 250-2,000 mg range. For arthritis, dosages of 8-60 g of fresh turmeric root three times daily or 400-600 mg of curcumin three times daily have been

recommended by oral route. For dyspepsia, 1.5 phytochemical and comparative study of Tulsi and turmeric for anti-microbial activity, 3 g of turmeric root is recommended. Preparations of the root should be standardized to contain not less than 3% curcumin and not less than 3% volatile oils. [24]

Adverse Effects: No significant toxicity has been reported following either acute or chronic administration of turmeric extracts at standard doses. At very high doses (100 mg/kg body weight), curcumin may be ulcerogenic in animals, as evidenced by one rat study. There are no reported adverse effects of curcumin or turmeric, except rare cases of allergic contact dermatitis. One case occurred as an occupational illness in a miller working in a spice shop.[25]. The proportion of turmeric oil constituents could vary depending on the crop's location. Nevertheless, no toxicity warning has been reported for any of the components of the oil extracted from turmeric. Methyl eugenol, a genotoxic carcinogen, is the sole constituent of turmeric leaf oil (~3%). It is not present in turmeric rhizome oil. Moreover, possible heavy metal contamination is negligible if the oil is extracted through steam distillation[26]

1.14 Anti-inflammatory activity of turmeric oil mediated silver nanoparticles: Background

Curcuma longa is a medicinal plant commonly known as turmeric and well known for its medicinal properties. Curcumin, the main constituent of turmeric. Curcumin is responsible for the biological activities of turmeric. Curcumin has potent anti-inflammatory activity.

Aim: In the present study, Anti-inflammatory activity of turmeric oil mediated silver nanoparticle was Carried out.

Materials and Methods:

Turmeric oil was obtained from Synthite Industries Limited, Kerala as a gift sample and silver nanoparticle was prepared using Turmeric oil. The synthesized nanoparticles solution was preliminarily characterized by using UV-visible spectroscopy. The colour change in reaction mixture (Silver nitrate solution + turmeric oil) was recorded by visual observation. The results were recorded for the graphical analysis.

Conclusion: It may be concluded from this study that turmeric oil mediated silver nanoparticles can be used as potential source of anti-inflammatory agent.[27].

II. CONCLUSION:

In conclusion, turmeric oil, primarily derived from the rhizome of the *Curcuma longa* plant, has demonstrated significant anti-inflammatory properties attributed to its active compound, curcumin. Numerous studies have highlighted its ability to inhibit various inflammatory pathways, reduce oxidative stress, and modulate immune responses. This natural oil shows promise not only in traditional medicine but also as a complementary approach in modern therapeutic applications for inflammatory conditions because of inadequate clinical trials, further high-quality studies are needed to firmly establish the clinical efficacy of the plant. Further research is needed to fully understand its mechanisms, optimal dosages, and potential side effects. As interest in natural remedies continues to grow, turmeric oil could play an essential role in the development of safe and effective anti-inflammatory treatments.

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