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## Formulation and evaluation of herbal tablet containing nyctanthes arbor-tristis leaves having antiarthritic activity

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#### Abstract

This study aimed to formulate and evaluate herbal tablets incorporating Nyctanthesarbor-tristis leaves, renowned for their potential anti-arthritic properties. The tablets were prepared using various excipients and evaluated for physicochemical properties, such as hardness, friability, disintegration time, and drug content uniformity. The results demonstrated the successful formulation of herbal tablets with desirable physicochemical properties and promising anti-arthritic activity, suggesting their potential as a natural alternative for arthritis management.

Keywords: Nyctanthesarbor-tristis, arthritis, herbal tablet

#### Introduction

Swelling or inflammation of one or more joints means arthritis. It more than describes 100 conditions that affect the joints, connective tissues, and tissues around the joint. Depending on the type of arthritis, symptoms vary but usually include stiffness and joint pain. Joint pain is struggled with by patients suffering from arthritis, and nearly half of all adults with arthritis experience pain that is persistent. It occurs more frequently in men than in women. It is an immuno mediated response due to inflammation of the synovial joint. Osteoarthritis and rheumatoid arthritis are two of the most common types. Despite considerable progress in the treatment of arthritis by NSAIDs and other drugs, these changes usually develop slowly and get worse over time. The search for newer drugs continues because the existing synthetic drugs have several limitations. Modern medicine has also started admitting that ayurveda and herbal medicine have a lot of positive influence on the treatment of arthritis. A large number of medicinal plants have been tested and found to contain active principles with curative properties against arthritis. Traditionally, inflammatory conditions like arthritis were treated using herbal plants both internally as well as externally.

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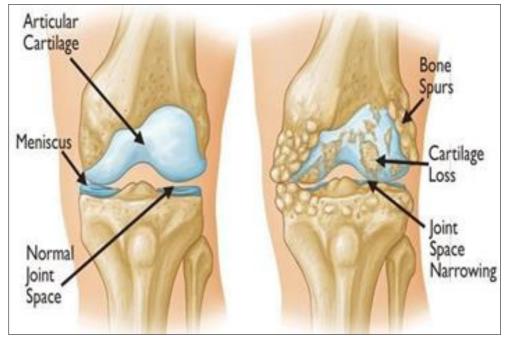


Fig 1: Normal joint and Arthritis Joint

#### **Etiology**

The etiology of arthritis varies with the type of arthritis. In osteoarthritis, the major contributory factors include advancing age, female sex, joint trauma, and obesity. Some genetic factors have been described such as mutations in genes encoding types II, IV,V, and VI collagens.

Rheumatoid arthritis (RA), on the other hand, is an autoimmune systemic inflammatory disorder. An-inter play between several genetic factors (HLADRB1 and others) and environmental factors (smoking) leads to activation and dysfunction of the immune system leading to inflammation in RA.

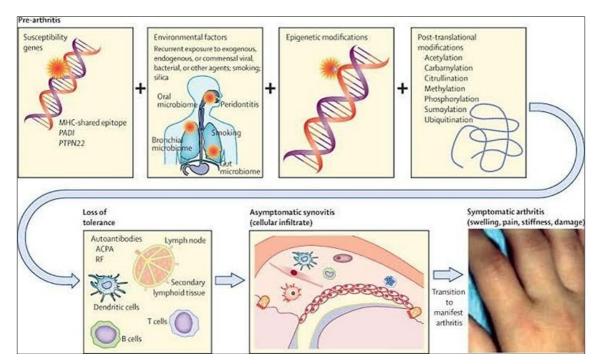


Fig 2: Etiolgical factors

About 1% of the world's population is afflicted by rheumatoid arthritis, women three times more often than men. Arthritis represents one of the most prevalent chronic health problems and is a leading cause of disability. Arthritis affected 43 million U.S. adults in 2002 and by the year 2020, this number is expected to reach 60 million 10. It is up to three times more common in smokers than non-smokers, particularly in men, heavy smokers, and those who are rheumatoid factor positive. A study in 2010 found that those

who drank modest amounts of alcohol regularly were four times less likely to get rheumatoid arthritis than those who never drank.

#### Types of arthritis

**Osteoarthritis:** Osteoarthritis (OA) is the most common form of arthritis. Some people call it degenerative joint disease or "wear and tear" arthritis. It occurs most frequently in the hands, hips, and knees.

#### Rheumatoid arthritis

Rheumatoid arthritis is an autoimmune disease. That means the immune system attacks parts of the body, especially the joints. That leads to inflammation, which can cause severe joint damage if you don't treat it. About 1 out of every 5 people who have rheumatoid arthritis get lumps on their skin called rheumatoid nodules

#### **Gout arthritis**

Gout is a common form of inflammatory arthritis that is very painful. It usually affects one joint at a time (often the big toe joint). There are times when symptoms get worse, known as flares, and times when there are no symptoms, known as remission. Having gout multiple times can lead to gouty arthritis, a form of arthritis which gets progressively worse.

#### Causes

There is no single cause of all types of arthritis. The cause or causes vary according to the type or form of arthritis. The cause of many types of arthritis is unknown. Researchers are looking into the role of genetics (heredity) and lifestyle int he development of arthritis.

#### Age

The older you get, you are more likely to develop most types of arthritis. Overtime, your joints tend to get worn down. That's why the risk of developing arthritis, especially osteoarthritis, goes up with age.

#### Gender

Most arthritis types are common in women, including rheumatoid arthritis and osteoarthritis. But, metabolic arthritis gout is more common in men than women.

#### Genes

Certain types of arthritis run in families. Conditions like rheumatoid arthritis, lupus, and ankylosing spondylitis, for example, are linked to certain genes. If your siblings or parents have these types of arthritis, you may also be at risk of developing it.

#### **Excess weight**

Being overweight puts extra stress on weight-bearing joints, increasing wear and tear and the risk of arthritis, especially osteoarthritis.

#### Inflammation

Inflammation is the body's normal healing mechanism that occurs to fight against bacterial, viral, or other reactions. There is no specific reason for Inflammation; it respond to injuries. The Inflammation Results in swelling, pain, and stiffness in the joints. Some of the inflammatory arthritis conditions are rheumatoid arthritis, reactive arthritis, ankylosing spondylitis and psoriatic arthritis.

#### **Degeneration**

Degeneration of cartilage leads to generative arthritis. The Main role of cartilage is to cover the ends of the bones and to glide or move the joints. Degeneration of the cartilage leads to osteoarthritis.

#### Work

Somejobsthatuserepetitivemovementsorheavyliftingcanstres sthejointsorcauseaninjury, which can lead to arthritis, particularly osteoarthritis. For example, if you need to do a lot of knee bends and squats at work, you might be more likely to get osteoarthritis.

#### **Symptoms**

**Pain:** Arthritis pain may intermittent (come and go) or persistent (constant).

#### Swelling

Usually, in arthritis conditions, joints become swollen and feel warm or tender to the touch.

#### Stiffness

When you wake-up or after you've been sitting for a while.

#### **Tenderness**

the area is sorewhen you touch it Lack of movement the joint won't complete its full range of motion

#### Grating

You might feel things rubbing to get her inside the joint.

#### Bone spur

Lump of bone forms around the joint pain, swelling and tenderness for 6 weeks or longer Morning stiffness for at least 30 minutes.

#### **Diagnosis**

Arthritis is diagnosed by reviewing symptoms, conducting a physical examination, and doing X-rays and lab tests. It's best to diagnose arthritis early within 6 months of the onset of symptoms so that people with the disease can begin treatment to slow or stop disease progression (for example, damage to joints). Diagnosis and effective treatments, particularly treatment to suppress or control inflammation, can help reduce the damaging effects of arthritis.

#### **Conventional Treatment**

**Medication:** Anti-inflammatory medications to provide pain relief and lower inflammation. Corticosteroids that can help decrease inflammation, provide some pain relief, ands low joint damage. Because they are potent drugs and have potential side effects, your doctor will prescribe the lowest dose possible to achieve the desired benefit. Disease-modifying anti-rheumatic drugs (DMARDs) that can help to slow or change the progression of the disease.

#### 1. Surgical treatment

Arthroscopy, Joint replacement Cartilage grafting, Joint fusion Synovectomy, Osteotomy Total joint replacement (TJR) that includes knee replacement, shoulder replacement, ankle, and hip replacement.

#### 2. Conservative or non-surgical treatment

Lifestyle modifications, Home remedies for arthritis Physical therapy, Occupational therapy. Heat and cold therapy using the ideal pads, Massage therapies.

#### **Plant Profile**



Fig 3: Nyctanthes arbor-tristis plant

#### Scientific Classification of Nyctanthes Arbor-tristis

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Lamiales
Family	Oleaceae
Genus	Nyctanthes
Species	Arbor-tristis
Binomial Name	Nyctanthesarbor-tristis

Synonym: Night-blooming jasmine, Parijat, harsingar

#### Geographical source

Nyctanthes arbor-tristis Linn is native to India, distributed widely in sub-Himalayan regions and southward to Godavari. It is also widely distributed in Bangladesh, Indo-Pak subcontinent and South-East Asia, tropical and subtropical South East Asia. It grows in Indo-Malayan region and distributed across Terai tract swell as Burma and Ceylon. I Tolerate Moderate Shade and is often found as under growth in dry deciduous forests. It is also found in Thailand.

Chemical constituents: Leaves of Nyctanthes arbor-tristis contains the following chemical active constituents. Flavanol glycosides, D-mannitol, β-sitosterol, Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, Ascorbic acid and Tannic acid etc. are few important phytochemical constituents that has been reported so far. Essential oils, Nyctanthin, D-mannitol, Glucose, Tannin, gentiobioside of crocin- 3 and crocin 1, β-D monoglucoside ester of α-crocetin and carotenoids. Seeds of this plant consists of palmitic and myristic acids, arbortristoside A&B, Glycerides of linoleic acid, stearic acid, nyctanthic acid, 3-4 secotriterpene acid, oleic acid, lignoceric acid and a water dissolvable polysaccharide made out of D-mannose and Dglucose. The bark of Nyctanthes arbor-tristis comprises of alkaloids and glycosides. Naringenin-4-0- β-glucapyranosylα-xylopyranoside and β-sitosterol are present, that have been isolated from the stem of the plant. Flower oil consists of different important phytoconstituents like anisaldehyde, phenyl acetaldehyde, terpenoids, and other ketones. It also consists of polysaccharides, phenyl propanoid glycoside, nyctanthoside- A, nyctanthic acid, friedelin and oleanolic acid and iridoid glycosides arbortristosides A, B and C, etc. among other important phytoconstituents.

#### **Morphological Character**

Nyctanthesarbor-tristis Linn is a large shrub growing to 10m tall, with flaky grey bark, stiff whitish hair, young branches and rough leaves. The flowers are fragrant, with a five to eightlobed white corolla with anorangered centre; they are produced in clusters of two to seven together, with individual flowers opening at dusk and finishing at dawn. Calyx is 6-8mm long, narrowly campanulate, hairy outside, glaborous insidetruncate or obscurely toothed or lobed, ciliated. Corolla glaborous and is more than 13 mm long; tube is 6-8mm long, orange coloured, about equalling the limbs; lobes are white and unequally obcordate and cuneate. The leaves are opposite, simple, 6-12 cm long and 2-6.5 cm broad, with an entire margin. The fruit is a flat brown heartshaped to round capsule 2 cm diameter, with two sections each containing a single seed. These are long and broad, Obcordate or nearly orbicular, compressed, 2-celled. Seeds are exalbuminous, with a thick testa. The outer layer of large transparent cells is heavily vascularized.

#### **Antibacterial activity**

Antibacterial activity of lower, leaf, seed, and fruit ethyl acetate and chloroform extracts against gram-positive and gram-negative bacteria was investigated. Both ethyl acetate and chloroform extracts showed significant antibacterial activity against the bacteria tested. Flower ethyl acetate and seed chloroform extract exhibited broad-spectrum antibacterial activity against both gram-negative and gram-positive bacteria, while leaf extract showed antibacterial activity against only gram-negative bacteria. Fruit and seed ethyl acetate extracts, while flower and seed, revealed the

presence of phytosterols, phenolics, tannins, flavonoids, glycosides, and saponins. Phenolic compounds and tannins were found to be active against the bacteria. Tannins have been found to form irreversible complexes with proline-rich proteins, resulting in the inhibition of cell protein synthesis and playing an important role as stable and potent antioxidants, astringents, and in the treatment of diarrhea and dysentery.

#### **Anti-fungal activity**

Different parts of NAT plant were examined for antifungal activity against three most prevalent clinical pathogenic fungi *Aspergillus niger*, Penicillium and Aspergillus flavus. Fresh and mature leaves, seeds, stem, bark and flowers were collected and dried, and extraction was performed with distilled water, methanol and chloroform. The antifungal activity of the extracts was measured by well diffusion method in terms of "Zone of inhibition" of fungal growth. The results revealed that only the distilled water extract of stem and bark of NAT showed antifungal activity against A. niger, while the chloroform extract of leaves was only effective against flavus. The study showed that the most effective results for antifungal activity was shown by methanolic extract of leaves.

#### Analgesic and anti-inflammatory activity

The pathophysiological response of mammalian tissue towards various hostile agents such as in factious organisms, toxic chemicals, physical injury or tumor growth is called inflammation. Edema formation, leukocyte infiltration and granuloma formation are components of inflammation.

Glucocorticosteroids and non-steroidal anti-in flammatory drugs (NSAIDs) are the two main type so fanti-in flammatory agents but due to their adverse side effects various alternatives of NSAIDs and opiates are being searched all over the world. NAT Was examined for the same, and experiments were carried out on various animal models. The methanolic extract of NAT stem bark showed the analgesic and anti-inflammatory activity by preventing stimulation of nociceptive components which may happened due to the inhibition of the production of Prostaglandin and related compounds. Experimental results also showed that the extract reduced the rate of edema in carrageenan-induced rat paw edema model.

#### Anti-arthritic activity

Methyl, ethyl acetate and n-hexane extracts of mature leaves of NAT were examined for anti-arthritic activity using rat model of FCA-induced arthritis. The comparative study of extracts showed that the ethyl the acetate extract of NAT leaves was most promising than others. The ethyl acetate extract showed maximum inhibition of paw edema as compared to the other two extracts. It more significantly attenuated infiltration of inflammatory cells in the ankle joint, total leukocyte count, and reduction in bone erosion.

#### Antioxidant activity

The *invitro* anti-oxidant activity of *N.arbor-tristis* was carried out using 1,1-diphenyl-2- Picrylhydrazyl (DPPH), hydroxyl, and superoxide radicals, and hydrogen peroxide scavenging assays. The plant has a reducing power which is attributed to high phenolics and flavonoid contents. Leaves show concentration-dependent free radical scavenging activity in *in vitro* DPPH assay assessment of free radicals. In another study, the totalphenolic content in the methanolic extract of the leaves was also analysed using other *in vitro* anti-oxidant studies and was established as the important chemical component for the antioxidant.

### Medicinal Usage of Various Partsof NatIn Ayurveda, Siddha and Unani System

Nyctanthes arbor-tristis has been used by tribal people of India (Orissa and Bihar) along with its use inAyurveda, SiddhaandUnanisystemofmedicinesformanyyears. Variousph armacologicalactionsofdifferentparts of plant have been investigated. Seeds are used as anthelminthic, in alopecia, bilious pyrexia and powdered form is used for curing scurfy affections of scalp, piles and skin diseases. Powdered stem bark is given to patients with rheumatic joint pain, used as an expectorant, in treatment of malaria, snake bite, bronchitis, ulcers, bleeding gums, anorexia, liver disorders, piles, worm infestation, blood disorder, oliguria, skin diseases and fever. Stem bark pounded with Zingiber officinale and Piper long um is boiled in water and the resultant liquid is taken for two days for treatment of malaria while the resultant paste on mixing with Arjuna bark is rubbed on the body for treatment of internal injury and joint broken bones. The oil preparedout of the bark of the plant is mixed with rice gruel and rock salt to prepare adose form (called anjana in ayurveda) used to apply in sclera of eye is found to be beneficial for various eye diseases. Leaves are used for the treatment of various diseases such as obstinate sciatica, chronic pyrexia, rheumatism. intestinal worminfection, anorexia. haemorrhoid, liver disorders, biliary disorders, pyrexia with rigors, and as laxative, diaphoretic, diuretic and antidote to reptile venom. Leaf succulent mixed in honey, given thrice daily is effective in cough. Paste of leaves with honey is also given for treatment of pyrexia, high blood pressure, diabetes and leaf juice with honey is used to curechronic fever and with loha-bhasma (mineral based ayurvedic medicine that contains elemental iron micro-fine particles prepared through the process of calcination under high temperature) is used in anaemia and hepato-biliary diseases (hepatic and spleen enlargement) while decoction of leaves is specifically recommended for obstinate sciatica.

#### Uses

Current study investigated the anti-arthritic potential of different extracts of N. arbor-tristis leaves. The data showed that all the extracts possessed ant-arthritic activities, plant is a reservoir of potentially useful active chemical entities which act as drugs as well as intermediates the whole plant possessed multiple pharmacological activities. Traditional medicine practitioners use leaf extract of Nyctanthes arbor-tristis for symptomatic relief of arthritis. Previous studies indicate the anti-inflammatory effect of flowers and seeds of the extract. Anti-inflammatory activity in leaves of Harsingar supports its use in various inflammatory conditions by the followers of the Ayurvedic system of medicine. The extract significantly reduced acuteinflammatoryswellinginthekneejoint. The presentresearc hisfocusonthe Arthritis, Nyctanthesarbor tristis leaves were proven activity to cure Arthritis and gives relief. From fever, pains and inflammation. The whole plant having various medicinal activities like anti-fungal, anti-diabetic, antioxidant.

#### **Materials and Methods**

Material: Herb: Nyctanthesarbor-tristis.

#### **Excipients**

Methyl cellulose, magnesium stearate, Talc, Lactose, Acacia.

**Distilled water:** Needed as a solvent

**Apparatus:** Beaker, Sieve no.22, Measuring cylinder, Mortar and Pestle, Stirrer.

#### Instruments

**Instruments:** Hot air oven, Mixer, Tablet punching machine, Analytical balance, Monsanto hardness tester, Vernier Caliper, Friabilator, Disintegration apparatus.

#### Preparation of dry powder of nyctanthus arbour tristis

The preparation of dry powder from Nyctanthesarbor-tristis leaves involves several steps to ensure the quality and efficacy of the final product. Initially, fresh leaves of Nyctanthesarbor tristis are meticulously collected from the local area to ensure their purity and potency. The collected leaves undergo thorough cleaning using distilled water to remove any impurities or contaminants.

Once cleaned, the leaves are then dried at room temperature for several days to reduce their moisture content and facilitate easier processing. Subsequently, a hot air oven is utilized to ensure complete drying of the leaves, as moisture can adversely affect the stability and shelf-life of the final powder.

After the leaves are thoroughly dried, they are carefully collected and ground into a fine powder using a mixer. This grinding process ensures uniformity and consistency in particle size, which is essential for the accurate dosing and effective extraction of active constituents during subsequent formulation processes.

Overall, the preparation of dry powder from Nyctanthesarbor-tristis leaves involves meticulous collection, cleaning, drying, and grinding steps to obtain a high-quality powder with optimal therapeutic properties for further medicinal applications.

#### Preparation of 1% /3% /5% of acacia solution

Take 100 ml of distilled water in a 3 beaker. Take 1gm, 3gm, 5gm of acacia powder in respective beaker to the 100 ml of distilled water. Stir continuously until all the powder is thoroughly mixed.

#### Wet granulation method

Weigh all ingredients accurately, mix well and triturate by using mortar and pestle. The prepared 1% binding agent was added slowly to form a damp mass. Damp mass was transfer through sieve no. 22. Prepared granules are dried at room temperature. The well dried granules are ready for compression

#### Formulation of herbal tablets

In this formulation, the dried leaves powder of Nyctanthesarbor-tristis was used to form a tablet dosage form. The formulation was done by following the wet granulation process and further compression by ing tablet punching machine

Table 1: Composition of formulations

Sr. No	Ingredients	Quantity		
Sr. No		Formula 1	Formula 2	Formula 3
1.	Nyctanthesarbor tristis	250 mg	250 mg	250 mg
2.	Methyl cellulose	180 mg	180 mg	180 mg
3.	Magnesium stearate	20 mg	20 mg	20 mg
4.	Talc	10 mg	10 mg	10 mg
5.	Lactose	50 mg	50 mg	50 mg
6.	Acacia	1%	3%	5%

#### **Evaluation**

#### **Pre-formulation study**

**Bulk density:** Bulk density was carried out in 100 ml dried measuring cylinder. Pouring of dried granules in measuring cylinder and calculated by using the following formula; Bulk density = Mass of the granules/Bulk volume of the granules.

#### **Tapped density**

Tapped density was carried out by pouring of dried granules in 100 ml measuring cylinder.100 tapping was done, note down the volume and calculate by using the following formula;

#### Hausner's ratio

Hausner's ratio is the ratio of the tapped density of granules to the bulk density of granules. Calculated by using the following formula.

Hausner's ratio = Tapped density/Bulk density.

#### Carr's index

Carr's index or compressibility index is determined by the following

**Formula:** Carr's index [%] = Tapped density-Bulk density / Tapped density x100

#### Weight variation test:

**Test variation weight:** The procedure followed the weight variation test. X1, X2, X3, Weigh 20 tablets individually and consider them as X1, X2, X3, X20. Determine the weight average of 20 tablets X=(X1+X2+X3+X20)/20. The upper limit and lower limit compared the individual weight. No more than two of the tablets differ from the average weight by more than the % error listed, and no tablets differ by more than double that percentage.

#### Hardness and thickness test

**Thickness and hardness test:** For each formulation, the thickness and hardness of 20 tablets were determined. Hardness was determined by Monsanto hardness tester and tablets' thickness was determined by Vernier Calipers.

#### Friability test

**Tablets friability:** In a laboratory, the tablets' friability can be determined by Roche friabilator. The friabilator consists of a plastic chamber that rotates at 25rpm, dropping the tablets through a distance of six inches in the friabilator, which is then operated for 100 revolutions. The tablets are reweighed. Compressed tablets losing less than 0.5% to 1.0% of the tablet weight are considered acceptable.

#### Disintegration time

**Time disintegration:** This test was the time required for the tablet to separate into particles. The disintegration test measures only the time required under a given set of conditions for a group of tablets to disintegrate into particles. This test was performed to identify the disintegration of tablets in a specific time period

#### Result

The formulation of herbal anti-arthritic tablet was prepared by wet granulation method. Tablets were tested for preformulation studies and physical parameters were also evaluated.

All the evaluated pre-formulation parameters are shown in table 2.Based on the pre-formulation study the flow property of granules was good. The physical parameter were shown in table 3. The compressed tablet color was greenish grey for F1 and F3 and dark greenish grey for F2.

Table 2: Pre-formulation parameter for herbal tablet

Sr. No.	Pre formulation parameter	Formula1	Formula2	Formula3
1.	Bulk density	0.137gm/cm <sup>3</sup>	$0.14 \mathrm{gm/cm^3}$	0.19gm/cm <sup>3</sup>
2.	Tapped density	$0.165  \text{gm/cm}^3$	$0.12  \text{gm/cm}^3$	$0.24 \mathrm{gm/cm^3}$
3.	Carr's index	16.51%	10.12%	19.77%
4.	Hausner's ratio	1.21	1.66	1.29

Table 3: Physical parameter for herbal tablet

Sr. No.	Parameters	Formula 1	Formula 2	Formula 3
1.	Weight variation test	6%	5%	7.5%
2.	Hardness[kg/cm <sup>2</sup>	4	6	5
3.	Thickness[mm]	3.258	4.3312	4.3312
4.	Friability Test[%]	10.74	1.8	1.022
5.	Disintegration test[min]	19	25	21



Fig 3: Antiarthritic Herbal Tablet

#### Discussion

Nyctanthesarbor-tristis was a traditional medicinal plant which having various medicinal activities but present research was focused on Arthritis and antipyretic, analgesic and anti-inflammatory activity. The leaves powder was used to formulate tablets. Wet granulation was done by using different concentration of binders and making three batches like F1, F2, F3. Pre-formulation study was carried out and gives good flow properties of prepared granules. The compression of prepared tablets, were evaluated and gives satisfactory results. The batch F2 was more disintegration time as compare to F1 and F3.All the pre formulation and evaluation studies were performed.

#### Conclusion

Based on the results it is concluded that the formulation and evaluation are good. The pharmacological evaluation is required for the treatment of Arthritis.

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