



Development & Evaluation Of Ibuprofen Anti Inflammatory Cream

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ABSTRACT :

The creation and assessment of an ibuprofen-based anti-inflammatory cream specifically designed for the treatment of psoriatic and arthritis are the main objectives of this study. Psoriatic arthritis poses additional challenges because it also causes inflammation of the skin and joints. Arthritis is a common inflammatory joint disease that affects millions of people worldwide. The goal of the cream's formulation was to maximize ibuprofen's therapeutic benefit while reducing side effects. Ibuprofen was added to cream bases in varying concentrations, and the viscosity, pH, and stability of the mixtures were evaluated. The anti-inflammatory activity of the cream was assessed in vitro using appropriate cell models. The effectiveness of the cream in lowering inflammation and enhancing joint function was also evaluated through in vivo studies using animal models of psoriatic and arthritis. The development of an ibuprofen cream with desired physicochemical properties and strong anti-inflammatory effects was successfully demonstrated by the results. Additionally, the cream showed encouraging results in reducing the symptoms of arthritis in animal models, indicating that it may be a viable treatment option for people with psoriatic arthritis and arthritis. Additional clinical research is necessary to confirm its safety and effectiveness when used on human subjects.

Key words: rheumatoid arthritis, psoriasis arthritis, chronic inflammation, joint pain.

INTRODUCTION :

Skin

Skin disorders such as psoriasis, rheumatoid nodules, vasculitis, drug-induced skin reactions, and scleroderma can be brought on by arthritis. Psoriasis and psoriatic arthritis frequently coexist, resulting in red, scaly skin patches. Firm lumps under the skin that are common in rheumatoid arthritis are called rheumatoid nodules. Blood vessel inflammation brought on by vasculitis can manifest as skin lesions like ulcers or palpable purpura. [1]

Arthritis

Joint inflammation, which causes pain, stiffness, and decreased mobility, is the hallmark of many conditions collectively referred to as arthritis. Osteoarthritis (OA), rheumatoid arthritis (RA), psoriatic arthritis, gout, and ankylosing spondylitis are common varieties. OA causes the cartilage in weight-bearing joints to deteriorate. An autoimmune disease called RA targets the linings of joints. Urate crystal buildup, frequently in the big toe, is a symptom of gout. Psoriasis and psoriatic arthritis coexist, resulting in joint pain and skin symptoms. The main symptoms of ankylosing spondylitis are stiffness and fusion in the spine.[2]

Background information of Arthritis

More than 100 different medical disorders can be classified as arthritis. These disorders inflame joints, resulting in pain, edema, and decreased mobility. Age, heredity, obesity, and joint injuries are risk factors. A diagnosis is made using lab tests, imaging, physical examinations, and medical histories. The goal of treatment is to control symptoms and enhance quality of life by using medication, counseling, lifestyle modifications, and occasionally surgery. Even though there is no cure, there is hope for better treatments thanks to ongoing research. Overall, to reduce the effects of arthritis on health and quality of life, a thorough approach to diagnosis and treatment is necessary.[3]

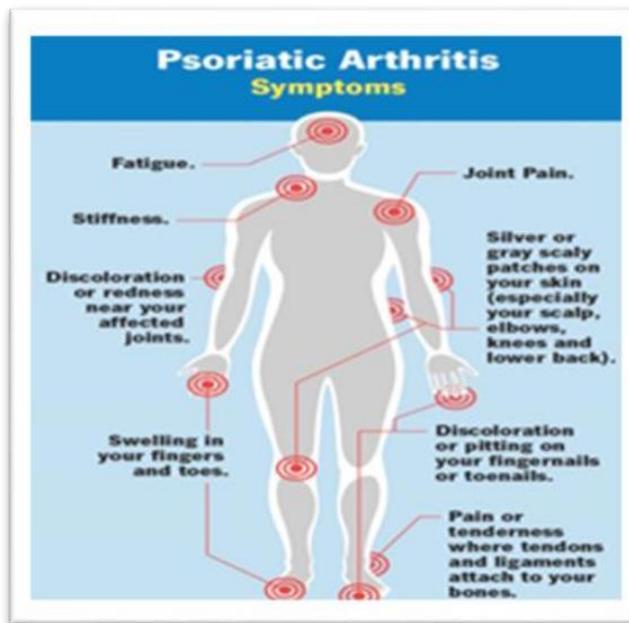
Psoriatic arthritis (PsA)

The inflammatory disease known as psoriatic arthritis (PsA) affects the joints and people who have psoriasis. It results in skin lesions, edema, stiffness, and joint pain. Although the precise cause is unknown, immunological, environmental, and genetic factors are involved. Exams, imaging, blood tests, and symptoms are used to make the diagnosis. With the use of medication, therapy, and lifestyle modifications, the goal of treatment is to lessen inflammation, ease symptoms, and avoid joint damage. Increasing knowledge and comprehension is essential for early identification and bettering results for PsA sufferers.[4]

Psoriatic arthritis symptoms

Joint pain, stiffness, and swelling are common symptoms of psoriatic arthritis (PsA), especially in the morning or after inactivity. Inflamed joints may become warm and red, and deformities may result from the inflammation. PsA is frequently accompanied by scaly, itchy skin lesions indicative of psoriasis. Discoloration and pitting of the nails are also common. Chronic inflammation is a common cause of fatigue. Reduced mobility and stiffness in the mornings get better with movement. Treatment for eye inflammation (uveitis/iritis) must be started right away. Mobility is restricted by tendon and ligament pain (tendonitis/enthesitis). Having less range of motion impacts day-to-day tasks.[5]

Fig no 3: Psoriatic Arthritis



Overview of Psoriatic Arthritis (PsA)

Epidemiology and Demographics

Psoriasis, a skin disorder characterized by red, scaly patches, is linked to psoriatic arthritis (PsA), a chronic inflammatory arthritis. PsA develops in about 20–30% of psoriasis sufferers, though it can also happen on its own. It can afflict people of any age, including children, but it usually begins in adults between the ages of 30 and 50.

Subtypes of Psoriatic Arthritis

Different subtypes of psoriatic arthritis (PsA) exist:

1. Asymmetric Oligoarticular: Consists of fewer than five joints distributed asymmetrically.
2. Symmetric Polyarticular: Resembling rheumatoid arthritis, it affects five or more joints symmetrically.
3. Distal Interphalangeal Predominant: Mostly impacts the joints in the distal fingers and toes.
4. Spondylitis: Like ankylosing spondylitis, this inflammation affects the spine and sacroiliac joints.
5. Arthritis Mutilans: a severe, quickly deforming form that results in deformity of the joints.[4]

Fig no 4: Types of Psoriatic Arthritis



Clinical Presentation

Psoriatic arthritis (PsA) typically affects the fingers, toes, wrists, knees, and ankles. It typically manifests as joint pain, swelling, and stiffness. Nail alterations and psoriasis lesions are examples of skin manifestations. Enthesitis, dactylitis, uveitis, and a higher risk of cardiovascular disease are examples of extra-articular characteristics.

Impact on Patients' Physical and Mental Well-being

Patients with psoriatic arthritis may experience major physical and psychological effects that impair their general health and quality of life. Prolonged joint pain, stiffness, and exhaustion can reduce range of motion, impede bodily functions, and cause disruptions to daily routines, professional endeavors, and social interactions. Psoriasis-related skin involvement can result in depression and psychosocial distress due to feelings of embarrassment, self-consciousness, and low self-esteem. Anxiety and stress can also be exacerbated by the unpredictable nature of disease flare-ups and the requirement for continuous care and observation. [5]

Epidemiology and Prevalence of Psoriatic Arthritis

Individuals with psoriasis, a common autoimmune skin condition characterized by red, scaly patches on the skin, are at risk of developing psoriatic arthritis (PsA), a chronic inflammatory arthritis. Comprehending the epidemiology and prevalence of PsA is crucial for efficient management and distribution of resources in global healthcare systems.

Global Prevalence Rates and Regional Variations

Global Prevalence Rates and Regional Variations: Estimates indicate that 20–30% of people with psoriasis go on to develop PsA, although prevalence rates vary throughout the world. Nonetheless, prevalence rates may vary greatly amongst populations and geographical areas.

Underdiagnosis and Misclassification Challenges

Misclassification and underdiagnosis continue to be major obstacles despite improvements in diagnostic criteria and raised public awareness of PsA. Numerous rheumatic and autoimmune diseases, including osteoarthritis, ankylosing spondylitis, and rheumatoid arthritis, can share symptoms and clinical manifestations with PsA. PsA may thus go undiagnosed and underappreciated, delaying the start of the proper course of care. Accurate diagnosis is also difficult due to the heterogeneous nature of PsA and the lack of particular diagnostic tests, especially in patients exhibiting mild or atypical symptoms. [6]

Burden of Psoriatic Arthritis

Individuals with psoriasis, a common autoimmune skin condition characterized by red, scaly patches on the skin, are at risk of developing psoriatic arthritis (PsA), a chronic inflammatory arthritis. Because of its high frequency, negative effects on quality of life, and related healthcare costs, PsA is acknowledged as a serious health concern.

Burden

Physical Burden: PsA impairs daily activities and results in disability, especially in weight-bearing joints where it causes joint pain, stiffness, and decreased mobility.

- **Psychosocial Burden:** Skin conditions associated with psoriasis can lead to social exclusion and humiliation. Anxiety and depression are exacerbated by flare-ups and the need for treatment, which affects relationships and productivity at work.
- **Healthcare Burden:** PsA necessitates regular doctor visits, specialist care, diagnostic testing, and a range of treatments, which raises medical expenses and reduces productivity.
- **Complications and Comorbidities:** PsA raises the risk of depression, osteoporosis, metabolic syndrome, cardiovascular disease, and metabolic syndrome, necessitating further medical care and resources. [7]

Pathophysiology of Psoriatic Arthritis :

Genetic Predisposition and Heritability Estimates

Psoriatic arthritis (PsA) is largely caused by genetic predisposition; heritability estimates range from 65% to 90%. Numerous susceptibility loci, including immune regulation genes like HLA-Cw*0602 and TNFAIP3, have been found through genome-wide association studies (GWAS), underscoring the complex genetic makeup of PsA.

Immunological Dysregulation

Immune dysregulation, including abnormal activation of both innate and adaptive immune pathways, is a feature of psoriatic arthritis (PsA). Pro-inflammatory cytokines such as TNF- α , IL-23, and IL-17 stimulate immune cells and proteolytic enzymes, which in turn cause synovitis, enthesitis, and bone erosion. In PsA, aberrant T cell responses, especially those of Th17 and Th1 cells, exacerbate chronic inflammation and promote joint pathology.

Environmental Triggers and Interaction with Genetic Susceptibility

Environmental factors that interact with genetic susceptibility to shape the clinical phenotype and severity of PsA include infections, smoking, obesity, stress, and other factors that may act as triggers or modifiers of the disease's onset and progression. For instance, immune responses may be triggered and inflammation may worsen in susceptible individuals by infections, especially those affecting the skin or gastrointestinal tract. Smoking may exacerbate the severity of the disease and has been linked to an increased risk of developing PsA. In addition to being linked to metabolic dysfunction and systemic inflammation, obesity is a risk factor for PsA and may play a role in the etiology of the disease.

Pathological Mechanisms

In PsA, synovitis and pannus formation are caused by inflammatory cells infiltrating the synovium and causing joint inflammation. An invasive, hyperplastic synovial tissue called pannus damages bone and cartilage, which leads to joint deformity and damage. One of the main characteristics of PsA is tendon insertion site inflammation, or tendonitis, which causes pain, swelling, and structural damage at these locations where tendons and ligaments attach to bone. Osteoclasts resorb bone matrix and cause bone erosion, which exacerbates joint destruction in PsA. [8]

Clinical Manifestations and Disease Phenotypes of Psoriatic Arthritis

Peripheral Arthritis

Asymmetric Oligoarthritis: One of the most common symptoms of early PsA is asymmetric oligoarthritis, which is defined as inflammation of fewer than five joints on different sides of the body. Over time, this condition can vary in pattern.

1. **Symmetric Polyarthritis:** Similar to rheumatoid arthritis (RA), this condition affects five or more joints symmetrically and, if left untreated, can cause serious joint damage.
2. **Distal Interphalangeal (DIP) Involvement:** This condition affects the distal joints of the fingers and toes and results in PsA-specific abnormalities like nail dystrophy and dactylitis.

Axial Involvement

Extra-Articular Manifestations

Classification Criteria

In addition to peripheral arthritis, PsA can also affect the axial skeleton, which includes the sacroiliac joints and spine. The axial involvement of PsA manifests as spondylitis, or inflammation of the spine, and sacroiliitis, or inflammation of the sacroiliac joints. People may experience back pain, stiffness, and reduced range of motion in their spines, all of which can lead to functional impairment and disability. Axial involvement is more common in patients with severe psoriasis, and it sometimes coexists with peripheral arthritis. [9]

Impact on Comorbidities and Quality of Life in Psoriatic Arthritis

Association with Cardiovascular Disease and Metabolic Syndrome

PsA is characterized by chronic inflammation, which increases the risk of cardiovascular disease (CVD) by causing endothelial dysfunction, plaque formation, and accelerated atherosclerosis. Traditional cardiovascular risk factors, also referred to as metabolic syndrome and including obesity, dyslipidemia, hypertension, and insulin resistance, are more common in PsA patients. Patients with PsA are more susceptible to heart attacks, strokes, and other cardiovascular events when these risk factors are combined with systemic inflammation. Furthermore, some PsA medications, like corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs), may make cardiovascular risk factors worse.

Association with Depression and Psychosocial Well-being

PsA is a chronic illness that can have a negative impact on psychosocial and mental health. Due to the unpredictable nature of the disease, pain, disability, and visible skin and joint involvement, patients may feel frustrated, anxious, depressed, and socially isolated. PsA patients may experience difficulties with their body image, low self-esteem, and social activity limitations, which can negatively affect their relationships, productivity at work, and general quality of life.

Impact on Physical Function and Work Productivity

PsA can seriously hinder daily living activities, mobility, and physical function. Patients may find it difficult to perform daily tasks due to limitations in their range of motion, muscle strength, and functional capacity caused by joint pain, stiffness, swelling, and fatigue. PsA patients may experience limitations in job performance due to pain, fatigue, and disability, as well as presenteeism and absenteeism from work. These factors may also have an impact on productivity. Additionally, PsA patients might experience stigma and discrimination at work, which would worsen their psychosocial distress and lower their quality of life. PsA patients may benefit from assistive technology, physical therapy, and rehabilitation programs in maintaining their independence and physical function.

Economic Burden on Healthcare Systems and Society

Due to direct expenses such as medication and medical services, as well as indirect costs like lost productivity and caretaker stress, psoriatic arthritis (PsA) presents a substantial financial burden. The cost of multidisciplinary care goes up even more. Reducing this burden and improving patient quality of life requires early diagnosis, efficient treatment, and thorough management plans. [10]

Diagnostic Challenges and Approaches in Psoriatic Arthritis

Importance of Early Diagnosis and Intervention

It is essential to diagnose psoriatic arthritis (PsA) as soon as possible to avoid permanent joint damage and disability. However, because PsA has a variety of clinical manifestations and is linked to psoriasis, diagnosing it can be difficult. A delayed diagnosis may result in deteriorating joint health and a lower standard of living. It takes alertness on the part of dermatologists and rheumatologists to identify and treat PsA in a timely manner.

Differential Diagnosis with Other Forms of Arthritis

It can be difficult to distinguish Psoriatic Arthritis (PsA) from other types of arthritis, such as Rheumatoid Arthritis (RA), Osteoarthritis (OA), and Ankylosing Spondylitis (AS), because these conditions share similar inflammatory pathways and overlapping clinical features. Accurate diagnosis depends on clinical assessment, which includes history, physical examination, and laboratory testing.

Role of Imaging Modalities

Imaging modalities are essential for the diagnosis and follow-up of PsA. These include radiography, ultrasound, and magnetic resonance imaging (MRI). Although it might not be able to identify early structural changes, radiography is frequently used to evaluate joint damage, including erosions, joint space narrowing, and periarticular osteopenia. Early identification of inflammatory changes in PsA is made possible by the greater sensitivity of ultrasound in detecting synovitis, tenosynovitis, and enthesitis compared to radiography. The most sensitive imaging technique for assessing PsA-related soft tissue inflammation, bone marrow edema, and enthesitis is magnetic resonance imaging (MRI), which offers important data for prognostication and treatment choices.

Biomarkers for Diagnostic and Prognostic Purposes

Although PsA lacks specific biomarkers, a number of laboratory tests can help with diagnosis and prognosis. In PsA, elevated levels of acute-phase reactants, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), may be a sign of systemic inflammation and disease activity. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies are examples of elevated autoantibodies that are usually absent in PsA but may be present in RA. The potential diagnostic and prognostic value of novel biomarkers, such as those related to cytokines, genetic factors, and bone turnover, is being studied in PsA. [11]

MATERIAL AND METHODOLOGY

Material-

Collection of material:-

All the mentioned chemicals, such as glycerine, sodium lauryl sulphate, citric acid, cetyl alcohol, and guar gum, can be found in ample supply at Pratibhatai Pawar College of Pharmacy in Shirampur.

Ibuprofen chemical from purchase Medical store Shirampur.[12]

Ingredient-

1. Glycerine
2. Sodium Lauryl Sulphate
3. Ibuprofen
4. Citric Acid
5. Cetyl Alcohol

6. Guar Gum

Methodology-**Formulation procedure:-**

1. Set Up Work Area: - Make sure all surfaces, tools, and supplies are clean and sterile for a sterile atmosphere.
2. Weigh the components:- To ensure consistency and efficacy, precisely measure each ingredient using a digital scale.
3. Heat the Water Phase: - In a heat-resistant container, combine the water and glycerin, and then gradually heat to 70–80°C (158–176°F).
4. Emulsify Ingredients: - Pour emulsifiers into the water phase and mix until they are evenly distributed and dissolved.
5. Incorporate Active Ingredient: Stirring continuously, add the active ingredients to the water phase gradually.
6. Thicken the Cream: - To thicken the mixture, sprinkle guar gum into the water phase and stir.
7. Cooling Phase: For ingredients that are heat-sensitive, allow the water phase to cool to 40–45°C (104–113°F).
8. Include the Oil Phase: - Mix and bring the components of the oil phase to the same temperature as the water phase.
9. Combine Phases: - Stir continuously as you gradually pour the oil phase into the cooled water phase.
10. Modify pH:- To adjust the pH of the cream as needed, dissolve the citric acid in the warm water and add it.
11. Cooling and Packaging: - Allow the cream to reach room temperature before transferring it to sterile containers, sealing them firmly, and labeling them with pertinent details. [13]

Table 1: Role of ingredients in Formulation

Ingredients	Role
Glycerine	Humectant & Moisturizer
Guar gum	Thickening agent & Stabilizer
Cetyl alcohol	Emolient & Skin Conditioning agent
Sodium lural sulphate	Emulsifier
Ibuprofen	Controlling swelling, pain & morning stiffness
Citric acid	pH Adjuster & Chelating agent
Tropocol (vit E)	Antioxidant
Water	Solvent

Table 3: Formula for preparation cream

Sr.No	Ingredients	F1	F2	F3	F4	F5
01	Glycerine	10ml	8ml	12ml	14ml	16ml
02	Guar gum	1.5gm	1.2gm	1.3gm	1.4gm	1.6gm
03	Cetyl alcohol	5gm	4gm	6gm	7gm	8gm
04	Sodium lural sulphate	1gm	0.8gm	0.6gm	0.7gm	0.8gm
05	Ibuprofen	5gm	4gm	4.5gm	6gm	7gm
06	Citric acid	0.5gm	0.4gm		0.6gm	0.7gm
07	Tropocol (vit-E)	2gm	1.6gm	2.4gm	2.8gm	2.9gm
08	Water	100ml	100ml	100ml	100ml	100ml

Evaluation parameters-

There are different types of evaluation test for Psoriasis Arthritis cream

1) Physical Characteristics

- a) Colour b) Odour c) Texture d) Appearance
- 2) Spreadability
- 3) pH
- 4) Viscosity
- 5) Stability
- 6) Skin Compatibility

1) Physical Characteristics:-

- a) Colour- White
- b) Odour- Neutral
- c) Texture- Smooth
- d) Appearance- Good

2) Spreadability:

1. Spread a tiny bit of cream over a level surface.
2. Spread the cream evenly using a spreading tool.
3. Calculate the cream's diameter or covered area.
4. Use the following formula to determine the spreadability: Spreadability = Area Covered by Cream / Applied Force.
5. Retest using several samples, then summarize the findings.

3) pH

1. First, adjust the pH meter.
2. Get the sample of cream ready.
3. Use the calibrated pH meter to determine the pH.
4. Note the pH reading.
5. To ensure accuracy, repeat.
6. Determine and report the average pH value.

4) Viscosity:

1. Get the cream sample ready and make sure it's the right temperature.
2. Make use of a viscometer meant for measuring cream viscosity.
3. Transfer the cream sample into the viscometer.
- Fourth, time how long it takes the cream to pass through the viscometer.
5. To ensure accuracy, repeat the measurement several times.
6. Determine the viscosity by utilizing the relevant formula.
7. Include the viscosity value and any pertinent observations in your report.

5) Stability:

- 1 First Assessment:
 - Examine the texture, color, scent, and appearance of the cream after preparation.
 - Take note of any variations from the expected traits.
2. Accelerated Stability Testing: - Expose cream to high temperatures (such as 40°C) for several weeks.
 - Keep an eye out for modifications to the viscosity, pH, color, odor, and microbiological growth.
3. Freeze-Thaw Cycling: - Alternately freeze cream (at, say, -20°C) and thaw it at room temperature. - After every cycle, check for variations in texture, appearance, or phase separation.[14]

RESULT & DISCUSSION :

The results underscore the topical cream's potential as a safe and efficacious treatment modality for PsA. By concurrently addressing joint inflammation and skin lesions, the cream offers holistic symptom alleviation and heightened patient well-being. The amalgamation of active pharmaceutical ingredients and skin-nourishing agents in the cream formulation synergistically augments therapeutic outcomes. Ibuprofen confers potent antiinflammatory and analgesic effects, while glycerine and vitamin E imbue the cream with moisturizing and soothing properties, mitigating dryness and discomfort. The cream's swift action and sustained relief render it a valuable adjunct to PsA management. Its localized application curtails systemic side effects commonly encountered with oral medications, fostering enhanced patient compliance and tolerance. Future research avenues may delve into further fine-tuning the cream formulation, exploring alternative active constituents, and conducting protracted efficacy assessments to gauge durability and safety in real-world clinical contexts. Collectively, the topical cream epitomizes a versatile and patient-centric approach to PsA therapy, heralding a promising stride towards improved patient outcomes and quality of life

Table 3: Results of Evaluation of Cream

Sr.No	Evaluation parameters	F1	F2	F3	F4	F5
01	Colour	White	Off White	Ivory	White	Creamy
02	Odour	Mild	Slight	Faint	Netural	Mild
03	Texture	Creamy	Grainy	Thick	Smooth	Silky
04	Appearance	Homogeneous	Homogeneous	Homogeneous	Homogeneous	Homogeneous
05	Spreadability	Easy	Moderate	Difficult	Easy	Moderate
06	pH	5.7	6.0	5.5	5.8	6.2
07	Viscosity	1200cP	950cP	1300cP	1100cP	1000cP
08	Stability	Stable	Stable	Stable	Stable	Stable

CONCLUSION :

The final formulation (F4) exhibited greater stability compared to formulations F1,F2, F3 and F5 achieved through error minimization. F4's antioxidant properties make it a promising candidate for large-scale production, benefitting both researchers and industries. This research project aimed to formulate and assess a cream for psoriatic arthritis. It provided insights into the disease's nature, symptoms, and factors contributing to its development. Pre-formulation studies for all three formulations met specifications, with subsequent evaluations covering color, odor, taste, and pH. The study highlights

the efficacy of the formulated cream compared to conventional treatments, emphasizing its potential as an effective remedy for psoriatic arthritis. Further research in this area is warranted to explore and optimize treatment options for this challenging condition.

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