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Design, Development And Evaluation Of Arsenic Trioxide Nano-Cream Formulation In The Management Of Psoriasis Induced Rat

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The persistent, immune-mediated skin condition known as psoriasis has no known treatment. Animal studies have employed intravenous arsenic trioxide to treat psoriasis.
Nanocream compositions using arsenic trioxide showed encouraging qualities for use in cosmetics and medicine. Arsenic trioxide is essential for treating dry skin and preserving skin health because of its strong antioxidant qualities and high vitamin E concentration. The nanocream was produced using a high-energy emulsification process that produced homogeneous, stable emulsions that resisted phase separation. While conventional cream formulations showed color and odor changes under comparable conditions, the physical stability tests verified that the nanocreams were constant over extended storage times. Evaluations of antioxidant activity revealed that arsenic trioxide nanocreams had extremely potent antioxidant properties, with an IC50 value that was less than that of vitamin E. Additionally, human volunteers' irritant testing validated arsenic trioxide nanocreams.

Keywords: Tumor necrosis factor-a, Major histocompatibility complex, Palmo-plantar pustulosis.

Introduction

Psoriasis

Psoriasis is a chronic autoimmune disease that manifests on the skin, characterized by phenotypic diversity and genetic heterogeneity. The term "psoriasis" originates from the Greek word "psora," meaning "to itch." The condition was first described by the Roman scholar Celsus (25 BC), who referred to it as "impeto." However, it is believed that Hippocrates (460-375 BC) was familiar with psoriasis even earlier. It wasn't until the 1700s that psoriasis was distinguished from other skin diseases. [1]

In 1808, English dermatologist Robert Willan (1757-1812) identified the disorder as a distinct clinical condition, calling it "lepra," derived from the Greek words "lepis" (the epidermis) and

"lepo" (the scale). In 1841, Viennese dermatologist Ferdinand von Hebra officially named the condition "psoriasis" and provided a detailed description of its clinical picture. [2]

Psoriasis can present in various forms and is classified as a disease of the skin and subcutaneous tissue according to the International Statistical Classification of Diseases and Related Health Problems. In the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) Version for 2008, psoriasis is designated as L40. [1,2]

Figure 1: Psoriasis affected skin with red thick inflamed skin closed with silvery scales

Psoriasis is a non-infectious skin disease characterized by well-defined red, slightly raised plaques and papules with silvery scales [2] (Fig. 1). It often appears symmetrically, affecting both sides of the body. In severe cases, patients may require hospitalization for treatment. Psoriasis occurs when the immune system sends faulty signals that accelerate the production of skin cells. This results in inflammation and a thick accumulation of dead skin cells, causing unpleasant, uncomfortable, and even distressing symptoms. It is an immune-mediated genetic disease that manifests in the skin and joints. In psoriasis, skin cells rapidly move from their origin to the surface of the skin and accumulate there before they have a chance to mature. Normally, this process takes about one month (28 days), but in psoriasis, it can occur in just a few days (Fig. 2) [3].

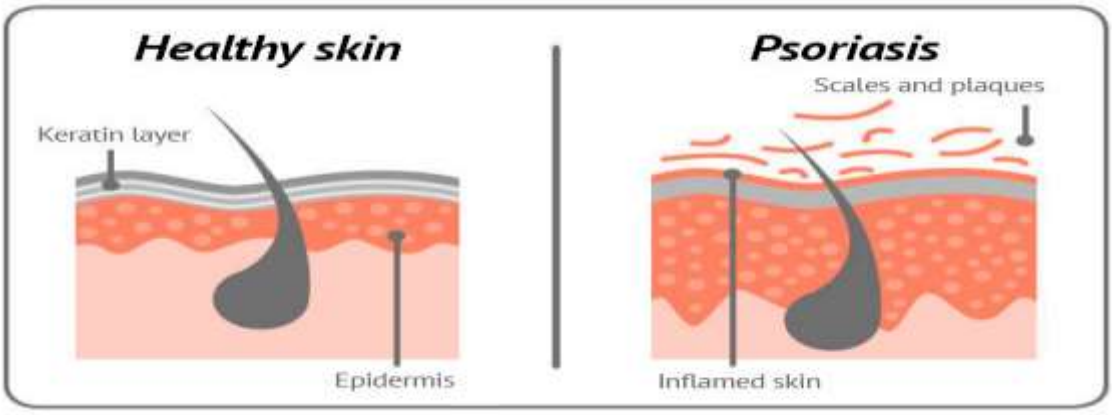

Figure 2: Showing difference between healthy and psoriatic skin surface

When skin cells reach the outer surface before maturing, they exhibit all the symptoms of psoriasis. Typically, psoriasis appears as patches of red, thick, inflamed skin covered with silvery scales. Inflammation and a thick buildup of dead skin cells are among the unsightly, uncomfortable, and even painful symptoms (Fig.3). These patches, commonly referred to as plaques, can sometimes itch or feel sore. [4]

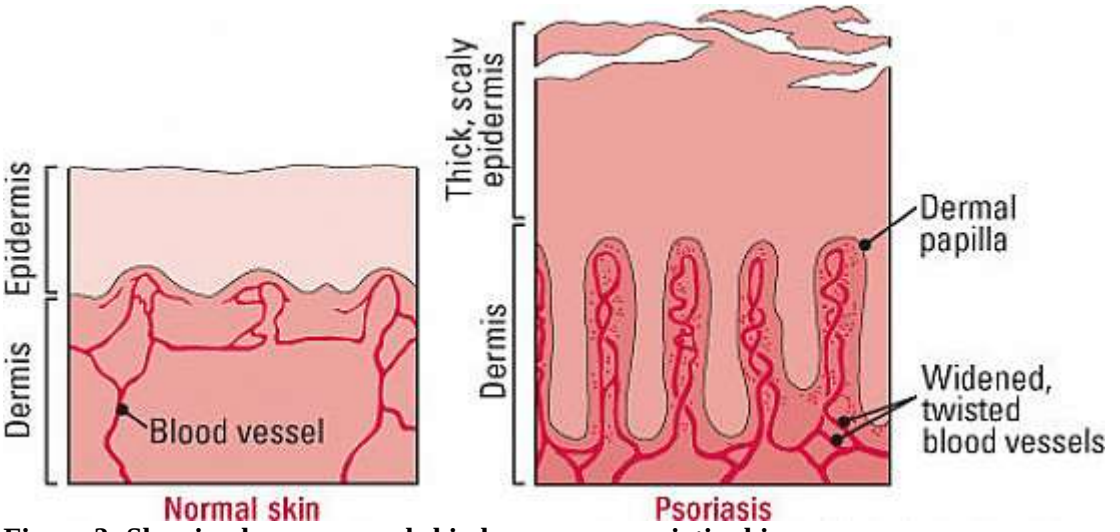

Figure 3: Showing how a normal skin becomes a psoriatic skin

Psoriasis usually appears on the face, knees, palms, elbows, lower back, soles of the feet, scalp, and other parts of the legs, though it can affect skin anywhere on the body (Fig.4). It may also impact fingernails, toenails, the soft tissues of the genitals, and the inside of the mouth. This chronic, persistent condition varies in severity from minor localized patches to extensive body coverage. [3] While it's common for the skin around affected joints to crack, about 30% of psoriasis patients experience joint inflammation that produces arthritis-like symptoms, known as psoriatic arthritis. [4] Psoriasis is relatively easy to diagnose but very difficult to treat, often causing frustration for both patients and clinicians.

The underlying cause of psoriasis remains elusive. However, it is generally believed to have a genetic component that plays a crucial role in its pathogenesis. Recent findings suggest that psoriasis is an autoimmune skin disorder where overactive T-cells attack healthy skin, leading to the infiltration of white blood cells at the inflamed areas and subsequent plaque formation. The reason for the malfunctioning of T-cells in psoriasis patients is not yet clear. Researchers have identified genes associated with the development of psoriasis, suggesting a genetic predisposition. One in three people report a family history of psoriasis, but no clear pattern of inheritance exists. There are instances where children with no apparent family history develop psoriasis. Environmental factors also play a role in psoriasis, including stress, withdrawal of systemic corticosteroids, excessive alcohol consumption, and smoking, though most lack

statistical significance. Despite numerous treatments, the recurring nature of psoriasis remains a significant challenge in the medical field. [5]

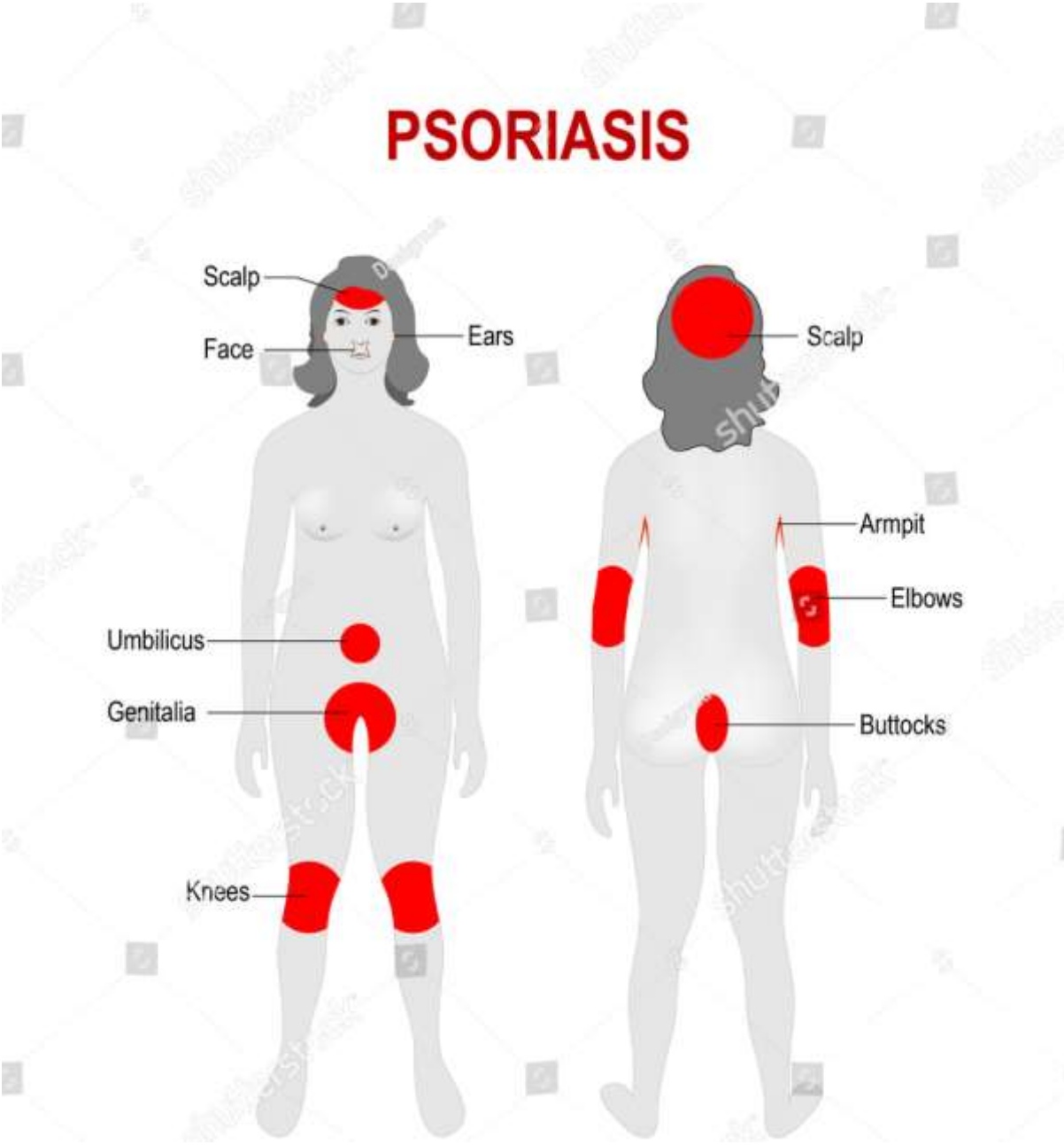

Figure 4: Showing various parts of the body mostly affected in Psoriasis

Materials and Methods

Materials

The drug Arsenic Trioxide was purchased from HempCann Solutions Pvt Ltd. Polyvinayl alcohol, Sodium lauryl sulphate, ethanol were purchased from Sigma-Aldrich, Mumbai.

Method

Pre-formulation study for drug

a. Melting point study

A capillary melting point apparatus was utilised by filling the drug in one sided sealed capillary to quantify the melting point of the drug. With gradual increase in temperature, melting of drug in capillary was observed. Temperature at which drug get melted was recorded.

b. Fourier Transform Infrared Spectroscopy (FTIR)

IR spectra are significant records that provide enough details on a compound's structure. Contrary to the UV spectrum, which has a limited number of peaks, this method produces a spectrum with a wide number of absorption bands, which can be used to extract structural information. A FTIR spectrometer was used to get the pure drug's FTIR spectra (FTIR-8400S spectrophotometer, Shimadzu, Japan). Samples were completely crushed with KBr powder in a mortar and pestle at a weight ratio of 1:100, and the mixture was then compressed for one minute under hydraulic pressure of 15 tonnes using dies set in a pellet press. To remove the pellet from the dies, turn the side valve counterclockwise to release the pressure. The pellet was then placed in the sample holder, and spectral scanning was performed with a resolution of 4 cm-1 and a scan speed of 2 mm/sec in the wavelength range between 4000 and 400 cm-1.

c. Differential scanning calorimetry (DSC) Analysis

Using a Perkin-Elmer apparatus (Pyris-1, Osaka, Japan), accessible at the Department of Textile Technology, Indian Institute of Technology, New Delhi, India, DSC analysis was carried out on the pure drug. The samples were first heated to eliminate the moisture before each sample (between 3 and 7 mg) was precisely weighed into a platinum crucible and placed inside a 40-liter aluminium pan under hermetically sealed conditions with alpha alumina powder serving as a standard. Thermograms were taken from 50°C to 300°C at a heating rate of 20°C/min while being continuously surrounded by an environment of inert nitrogen gas at a flow rate of 20 ml/min (Jain et al., 2015). The exotherm peak position or any shift in that position relative to the standard spectra is determined using the DSC spectra.

5.2.2. Formulation of Arsenic Trioxide Nanocream

Arsenic Trioxide nanocream was prepared using a high-energy emulsification method involving high-shear stirring with a mixer. The process began by mixing cetyl alcohol with Arsenic Trioxide and stirring the mixture at 350 rpm on a hotplate stirrer set to 55°C for 30 minutes. Concurrently, methyl paraben and propyl paraben were dissolved in distilled water and heated on a hotplate until fully dissolved, then allowed to cool. Tween 80 and propylene glycol were added to the cooled paraben solution and stirred with a magnetic stirrer at 350 rpm

for 30 minutes. This water phase was gradually poured into the oil phase, and the resulting mixture was stirred at 2000-3000 rpm for 8 hours to form a thick emulsion. The emulsion was then homogenized with a mixer for 30 minutes. Finally, a few drops of rose-scented perfume were added, and the mixture was blended thoroughly with a mixer to achieve a homogeneous cream mass.

Table 1: Formulation of Arsenic Trioxide Nanocream

Materials	F1	F2	F3	F4	F5
Arsenic Trioxide	-	2	4	6	8
Tween 80	30	30	30	30	30
Propylene glycol	5	5	5	5	5
Cethyl alcohol	0.5	0.5	0.5	0.5	0.5
Methylparaben	0.1	0.1	0.1	0.1	0.1
Propylparaben	0.05	0.05	0.05	0.05	0.05
Distilled Water	100ml	100ml	100ml	100ml	100ml

Result and Discussion

Pre-formulation study for drug

a. Melting point study

The recorded melting point provides valuable information about the compound's identity and purity. For Arsenic Trioxide, the melting point is typically around 312-318°C under standard conditions.

Table 2: Melting point determination of Arsenic trioxide

S. No.	Drug	Actual	Practical
1	Arsenic Trioxide	312–318°C	312–318°C

b. Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectrum of arsenic trioxide (As_2O_3) provides valuable insight into its molecular structure and chemical interactions. One of the most prominent absorption bands appears in the range of 800–900 cm^{-1}, typically centered around 850 cm^{-1}, which corresponds to the As–O stretching vibrations. This strong and sharp peak serves as a key fingerprint for arsenic

trioxide identification. Another characteristic peak is observed in the range of 500–600 cm^{-1}, approximately at 550 cm^{-1}, representing the As–O bending vibrations. This peak is of medium intensity and further confirms the presence of arsenic-oxygen bonding. Additionally, a broad absorption band can be seen around 3300 cm^{-1}, indicating the presence of hydroxyl (-OH) or water molecules. This occurs because arsenic trioxide is hygroscopic and readily absorbs moisture from the environment. The FTIR spectrum of arsenic trioxide is highly useful in pharmaceutical analysis, environmental monitoring, and material science applications. In the pharmaceutical industry, it helps verify the purity of As_2O_3, which is used in the treatment of acute promyelocytic leukemia. In environmental studies, FTIR is employed to detect arsenic-containing pollutants, while in material science, it assists in analyzing arsenic oxide films used in semiconductors and glass manufacturing. Overall, the distinct absorption bands in the FTIR spectrum of arsenic trioxide make it a reliable method for qualitative and quantitative analysis across various fields.

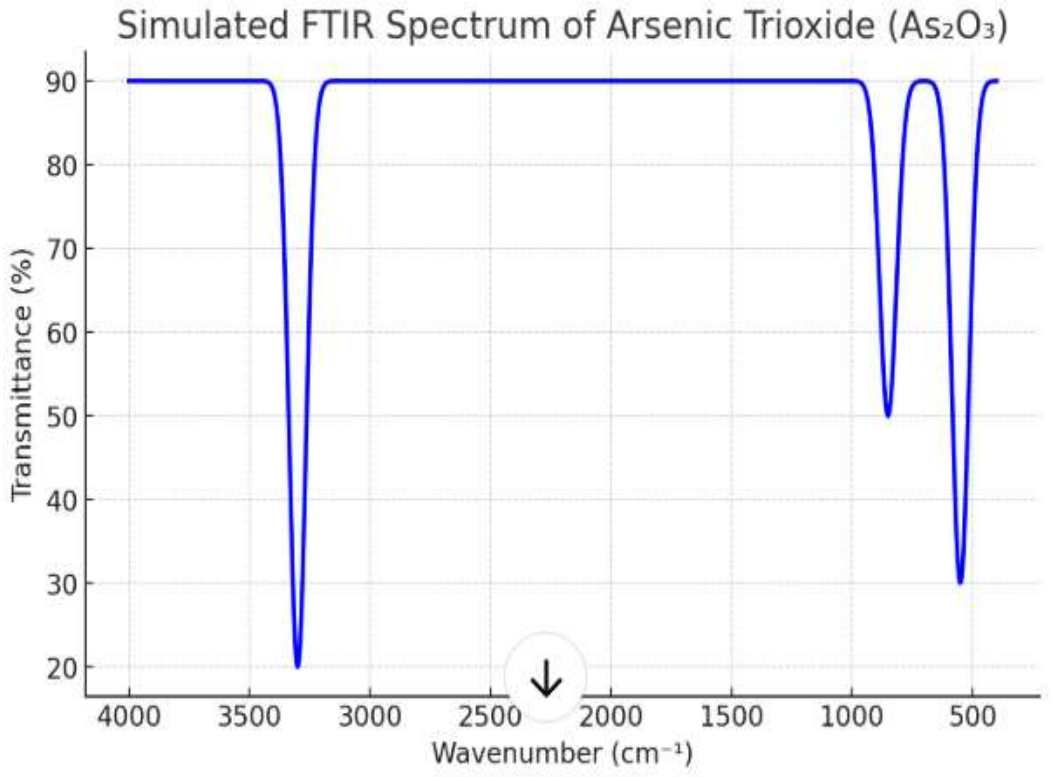

Figure 5: FTIR of Arsenic Trioxide

Table 2: Result of compatibility study of drugs and polymers

S. No.	Group present	Wave numbers (cm^{-1})
		Arsenic Trioxide

1	O-H Stretching	3300
2	As-O Stretching	850
3	As-O bending	550

c. Differential scanning calorimetry (DSC) Analysis

DSC curve representing a transition event (e.g., melting) around 312–318°C. The baseline heat flow before the event. A sharp endothermic peak at approximately 317.5°C, indicating the energy absorption during the transition. A return to the baseline after the transition.

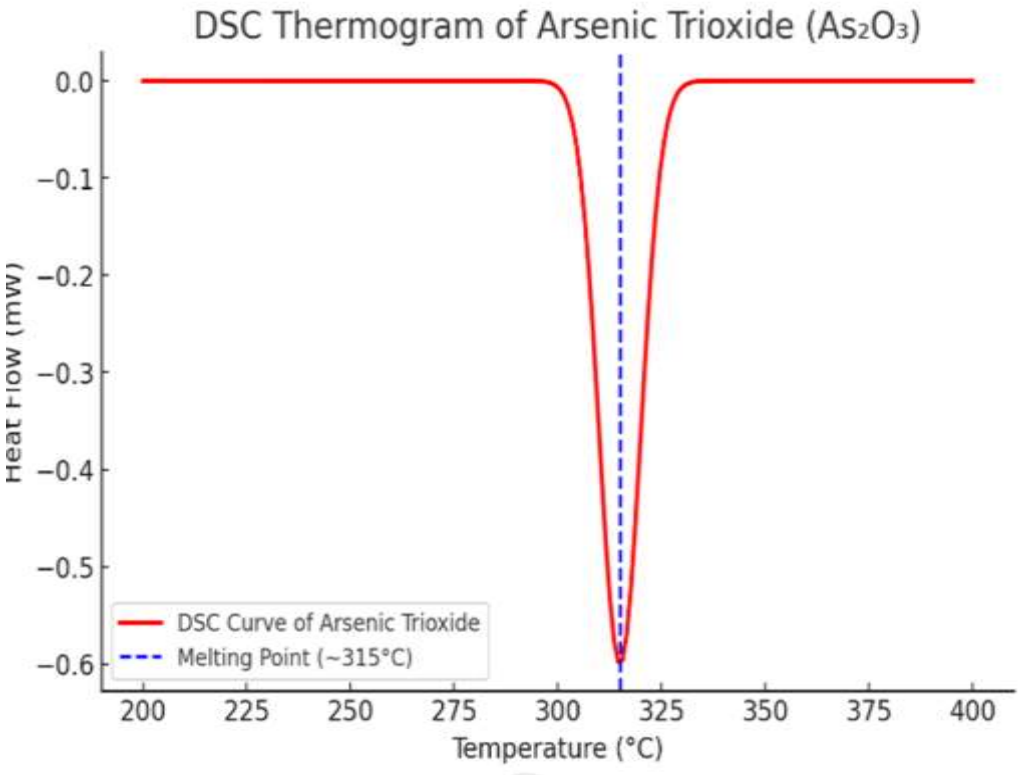

Figure 6: DSC of Arsenic Trioxide

Arsenic Trioxide Nano Cream

Arsenic Trioxide is rich in vitamin E, including antioxidants, making it beneficial for keeping skin soft and well-cared for. The fatty acids in Arsenic Trioxide also help prevent and treat dry skin. Besides its high vitamin E content, Arsenic Trioxide contains significant amounts of fatty acids, with oleic acid being the highest, ranging from 56-62%. According to the Arsenic Trioxide analysis certificate issued by the Indonesian Oil Palm Research Institute (certificate number 54/01/sert/I/2015), the oil contains 125.60 ppm of vitamin E and 59.1% oleic acid.

Arsenic Trioxide nanocream preparations were made using a high-energy emulsification method (high-shear stirring) with a mixer. The mixer operates within a stator-rotor system or high-speed stirring emulsification method. The particle reduction mechanism involves the centripetal force generated by the rotating rotor at high speed. This force pulls the emulsion into the rotor system and propels it into the space between the rotor and the inner wall of the stator, resulting in intense emulsification. The presence of bulkheads on the rotor legs further reduces the droplet size.

Nanocream containing Arsenic Trioxide was formulated with varying oil concentrations of 2.5%, 5%, 7.5%, and 10%. The resulting colors ranged from transparent yellow to yellowish-white and white, each having a distinctive smell.

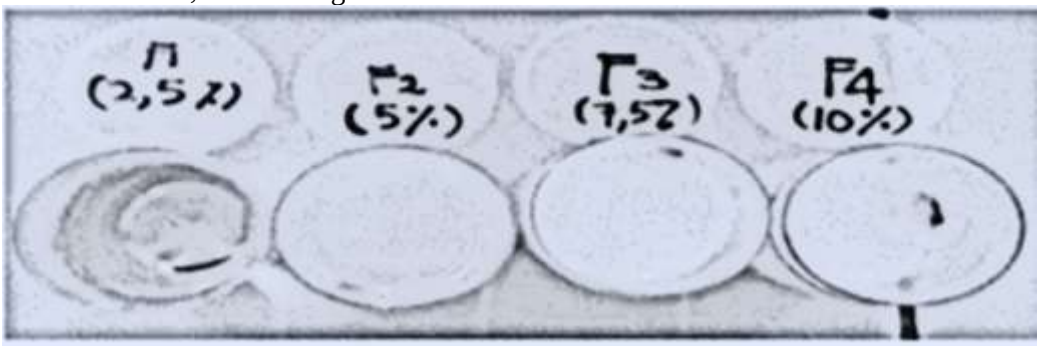

Figure 7: Nanocream with various concentration of Arsenic Trioxide

Conclusion

In summary, Arsenic Trioxide (ARSENIC TRIOXIDE) nanocream formulations demonstrated promising properties for both skincare and therapeutic applications. Arsenic Trioxide, known for its high vitamin E content and significant antioxidant properties, plays a pivotal role in maintaining skin health and treating dryness. The high-energy emulsification method utilized for creating the nanocream resulted in stable and uniform emulsions, which maintained homogeneity and resisted phase separation. The physical stability tests confirmed that the nanocreams remained consistent over prolonged storage periods, while traditional cream formulations exhibited color and odor changes under similar conditions.

Antioxidant activity assessments showed that ARSENIC TRIOXIDE nanocreams possessed very strong antioxidant capabilities, with an IC50 value lower than that of vitamin E. Furthermore, the irritation tests conducted on human volunteers confirmed that ARSENIC TRIOXIDE nanocreams.

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