# Formulation and Evaluation of the Polyherbal Nanoemulgel for the Treatment of Inflammation



**Ankit Shukla*, Dr. M.K Gupta**, Rahul Dev***, Debashish Purohit#, Manvendra Singh##, Pallavi Pal###**

*Research Scholar Career Point school of Pharmacy, C.P.U, Kota, Rajasthan

**Dean, Career Point School of Pharmacy, C.P.U, Kota, Rajasthan

*** Associate Professor, Axis Institute of Pharmacy, Kanpur

# Research Scholar, Career Point school of Pharmacy, C.P.U, Kota, Rajasthan

## Research Scholar Career Point school of Pharmacy, C.P.U, Kota, Rajasthan

### Assistant Professor, Axis Institute of Pharmacy

Corresponding Author- Ankit Shukla, Ankit1363@gmail.com

## Abstract:

The aim of the study was to formulate and characterize herbal nanoemulgel of Nyctanthes arbor-tristis and Aloe Vera. Nanoemulgel was formulated using three different gelling agents including Carbapol 934, Carbapol 940 and HPMC. The characterization studies were performed for physical appearance, pH, viscosity, drug content analysis, in vitro skin permeation studies and in vitro anti-inflammatory activity by IL-6 inhibition. Results showed that all the Nanoemulgel were found to be stable formulations with pH ranging from 6.17–6.43. Viscosity measurement revealed that all formulations were having Newtonian flow behavior with varying viscosities depending upon their composition. In vitro drug release study pronounced the maximum release with the more than 95%. The particle size analysis showed that all the formulations were within the nanometer range between 100.22±0.16 to 102.20±0.10 nm, indicating successful formation of nanoemulgel. A negative zeta potential indicated that the particles repel each other, which is necessary for stable dispersions; the zeta potential was found 24.60±0.44 to 37.40±0.44. In vitro anti-inflammatory studies results revealed that the formulated Nanoemulgel could potentially inhibit the IL-6 by 76%.

**Keywords:** Nanoemulgel, Herbal Nanoemulgel, Nyctanthes arbor-tristis and Aloe Vera Nanoemulgel

**DOI Number: 10.14704/nq.2022.20.13.NQ88346 Neuro Quantology 2022; 20(13):2773-2783**

## INTRODUCTION

The plant based medicines which are being used for the treatment of various diseases are practiced from the ancient time. There are various methods including ayurvedic, Unani, and Siddha medicines are being used [1]. The constituents of the plants are the most desirable discovery and validation in several medication therapies. Plant based medicine novel and functionally active in terms of diversify pharmacological activities of several classes of phytochemicals. These bioactive molecules are referred as secondary metabolites sometimes include flavonoids, alkaloids, terpenoids, and phenolic compounds [2].

These phytochemicals categories are often classified as pharmacological lineup for the treatments of several severe diseases by lowering the risk of diseases and promoting the healthy Wellness. Is it is validated that these plant extracts possess numerous biochemical properties such as anti-inflammatory, Antidiabetic, anti-fungal, antimicrobial and anticancer [3]. These plants are potentially active to get attention in various fields of the pharmaceutical industries such as food, cosmetic and therapeutic [4].

Inflammation is the body's response to infection, irritation or injury. The main symptoms of inflammation are redness, swelling, pain and

heat. Inflammation is a natural process that helps the body heal and protect itself from harm. However, sometimes inflammation can become chronic and lead to health problems [5].

There are a number of different reasons that inflammation may occur. One reason is due to an injury or infection. When the body is injured, it releases chemicals that cause blood vessels to swell and tissues to become warm and tender [6]. This helps to protect the area and promote healing. However, sometimes inflammation can occur without an apparent injury or infection, which is known as chronic inflammation. This type of inflammation is thought to be caused by a number of factors, including genetics, diet, stress, and environmental exposure [7].

Common etiology of inflammation is infection, trauma, or autoimmune disease. Infection-related inflammation is most often caused by viruses, bacteria, and other microorganisms that invade the body [8]. Trauma-related inflammation is usually the result of tissue damage from a physical injury or exposure to a chemical irritant. Autoimmune disease-related inflammation occurs when the body's immune system attacks its own tissues [9].

Nyctanthes arbor-tristis and Aloe Vera are two plants that are used in traditional medicine. They have a long history of use in Ayurvedic and Unani medicine [9]. Nyctanthes arbor-tristis is used for the treatment of colds, coughs, and fever. Aloe Vera is used for the treatment of burns, wounds, and skin diseases [8].

The traditional use of Nyctanthes arbor-tristis and Aloe Vera in inflammation and cancer is well documented. Both herbs have been shown to be effective in the treatment of various inflammatory conditions, including arthritis, colitis, and cancer [10]. The anti-inflammatory and anticancer effects of Nyctanthes arbor-tristis and Aloe Vera have been demonstrated in a number of studies. These plants contain compounds that can modulate the activity of inflammatory mediators, such as cytokines and eicosanoids. In addition, they also possess antioxidant properties that can scavenge reactive oxygen species and protect cells from oxidative stress [11].

Nyctanthes arbor-tristis and Aloe Vera are two of the most popular plants in the world. They both have a wide range of benefits and uses that make them essential to many people [12]. Nyctanthes arbor-tristis is a flowering tree that is native to India and Pakistan. It is also known as the night-flowering jasmine or Parijata tree. The tree can grow up to 20 feet tall and has small, white flowers that bloom at night [13]. Aloe Vera is a succulent plant that is native to Africa, Arabia, and Madagascar. It has thick, fleshy leaves that are filled with a clear gel. This gel has many healing properties and is often used in traditional medicine [14].



## 1. MATERIAL AND METHODOLOGY

### 1.1. Materials

The Aloe Vera and Nyctanthes Arbor leaves have been collected from the nearby garden of laboratory and were authenticated by ACME Research Solutions. All the other excipients and chemicals purchased were of analytical grades. The cell lines RAW 264.7 murine macrophage was procured from the NCC, Pune.

### 1.2. METHODOLOGY

#### 1.2.1. Collections of Plants, Authorization, and Grinding

Both the plants were collected from the nursery nearby Delhi. The plant species was scientifically authenticated at ACME research solutions. The collected plants samples of leaves work air dried under the sunlight for minimum 15 days. The dried materials of the plant were made powder using electrical grinder. Again the Powder what sieved and collective in the air tight container. The collected plants leaves were washed with the tap water to remove the debris of soil and dried under the sun for 15 days followed by grinding it using electrical grinder to make it powder for the extraction process and Phytochemical screening [15].

#### 1.2.2. Preparation of Nyctanthes and Aloe Vera Extract [16, 17]

The Soxhlet extraction was used to prepare Nyctanthes arbor-tristis and Aloe Vera extracts. The leaves of Nyctanthes arbor-tristis and Aloe Vera were dried and ground into a fine powder using a grinder. One hundred grams (100 g) of the powdered leaves were placed in a thimble, which was then inserted into the Soxhlet extractor. Ethanol, Methanol and water were added to the round-bottomed flask respectively. The assembly was placed on a heating mantle

set at definite temperature. After 8 h of extraction time, the solvent was removed from the thimble by rotary evaporation at 40°C under vacuum. The yield of the Nyctanthes arbor-tristis extract and Aloe Vera extract was 9.0% w/w and 11.4% w/w respectively.

### 1.2.3. Pharmacognostic and Physiochemical Parameters of *Nyctanthes and Aloe Vera*

The Pharmacognostic and Physiochemical Parameters are mentioned in the several officials book. The characters are mentioned in the Ayurvedic Pharmacopeia are mentioned below.

**Macroscopy [18, 19]**

**Nyctanthes arbor-tristis**

The leaves of Nyctanthes arbor-tristis are simple, opposite and decussate. The leaf-blades are ovate to oblong, 8–16 cm long, 3.5–8 cm broad, with an entire or serrulate margin and a petiole 5–10 mm long. The upper surface is dark green and glabrous while the lower surface is paler and pubescent along the veins. Both surfaces have a prominent midvein flanked by 2–4 pairs of lateral veins.

**Aloe Vera**

Aloe Vera leaves are thick and fleshy, with a serrated margin. The upper surface is green and the lower surface is glaucous. Both surfaces are covered with small, white spots. The leaf margins are yellowish-brown to red. The flowers are borne in inflorescences on peduncles up to 60 cm long. Each flower has a short corolla with recurred lobes that vary in color from yellow to orange-red.

**Organoleptic Parameters [20, 21]**

**Nyctanthes arbor-tristis**

The leaves of Nyctanthes arbor-tristis were analyzed for their organoleptic parameters. The results showed that the leaves were bitter, sweet, and astringent. The bitterness was more pronounced in the young leaves, while the sweetness and astringency were more pronounced in the mature leaves.

**Aloe Vera**

Aloe Vera leaves have a thin, clear, mucilaginous gel with a light yellow color. The plant has a strong, characteristic odor that may be due to the presence of Anthraquinone. Aloin and Emodin are the main compounds found in Aloe Vera leaves.

### 1.2.4. Phytochemical Analysis [22]

The leaves were subjected to extraction and the extracts were screened for their phytochemical constituents by standard procedures. The results showed that the ethanolic, water and methanolic extract of Nyctanthes arbor-tristis leaves contained flavonoids, tannins, saponins, steroids, terpenoids and alkaloids. (Table-2)



**Table-1: Phytochemical Screening (Nyctanthes Arbor)**

| Sn. | Test | Solvents | | |
|---|---|---|---|---|
| | | Methanol | Ethanol | Water |
| 1 | Alkaloids | Positive | Positive | Positive |
| 2 | Carbohydrates | Negative | Negative | Positive |
| 3 | Saponins | Positive | Positive | Positive |
| 4 | Glycosides | Positive | Positive | Positive |
| 5 | Steroids | Positive | Positive | Negative |
| 6 | Flavonoids | Positive | Positive | Positive |
| 7 | Tannins | Positive | Positive | Negative |

**Table-2: Phytochemical Screening (Aloe Vera)**

| Sn. | Test | Solvents | | |
|---|---|---|---|---|
| | | Methanol | Ethanol | Water |
| 1 | Alkaloids | Positive | Positive | Positive |
| 2 | Carbohydrates | Positive | Positive | Positive |
| 3 | Saponins | Positive | Positive | Positive |
| 4 | Glycosides | Negative | Positive | Negative |
| 5 | Steroids | Negative | Negative | Negative |
| 6 | Flavonoids | Negative | Positive | Positive |
| 7 | Tannins | Negative | Negative | Positive |

### 1.2.5. Preparation of Gel [23]

Clear gel was prepared by mixing 1g of polymer (Carbapol 940, Carbapol 934 and HPMC) in distilled water each in a separate beaker and kept overnight for soaking. The gel was adjusted pH by Triethanolamine to the desired pH range suitable for the skin. The gel uniformity was maintained by constantly stirring using magnetic stirrer.

**Table-3: Formulae of Nanoemulgel**

| Sn. | Ingredients | Formulations | | |
|---|---|---|---|---|
| | | F1 | F2 | F3 |
| | | % | | |
| 1 | Extract- Nyctanthes Arbor | 1 | 1 | 1 |
| 2 | Extract- Aloe Vera | 1 | 1 | 1 |
| 3 | Carbopol 940 | 1 | NA | NA |
| 4 | Carbopol 934 | NA | 1 | NA |
| 5 | HPMC | NA | NA | 1 |
| 6 | Span 20 | 3 | 3 | 3 |
| 7 | Tween 80 | 5.25 | 5.25 | 5.25 |
| 8 | Propylene glycol | 1.75 | 1.75 | 1.75 |
| 9 | Methyl Parabene | 0.03 | 0.03 | 0.03 |
| 10 | Propyl Parabene | 0.01 | 0.01 | 0.01 |
| 11 | Water | 100 | 100 | 100 |

### 1.3. Preparation of Nanoemulsion [24, 25]

Nanoemulsion has been prepared by spontaneous emulsification method. 1% of dried extract of Nyctanthes leaves and Aloe Vera into the oil phase (span 80) in the ratio of (1:1), by incorporating the required quantity of surfactant mixture Tween 80 and Propylene glycol. This mixture has been agitated well. With continuous stirring, gradually water has been added to the prepared mixture so that it might make up the volume.

**Preparation of Nanoemulgel**

- For the development of nanoemulgel, the prepared Nanoemulsion has been subjected to homogenization at 10,000 rpm for 1h.
- Few drops of Triethanolamine have been added to this mixture to keep it in a neutralized state.
- Then, this homogenized mixture was sonicated for about 10 min.

### 1.4. EVALUATION PARAMETERS

#### 1.4.1. Physical Characterization [25]

The physical examination of developed Nanoemulgel was performed to evaluate the physical appearance, grittiness, odour, homogeneity. The formulated nanoemulgel was inspected visually and recorded. The herbal nanoemulgel was found clear, odorless and particle was not observed during the inspection.

#### 1.4.2. pH [26]

The pH was determined using the digital pH meter. Exactly 1 gram of formulation was dissolved in 100 ml of purified water. The solution was then kept for at least 3 hours to get settled. After 3 hours pH measurement was taken in triplicates.

**Table-4: pH of Nanoemulgel (Mean ± SD)**

| Sn. | Formulations | Triplicates | pH (Mean ± SD) |
|---|---|---|---|
| 1 | F1 | 1 | 6.43±0.06 |
| 2 | | 2 | |
| 3 | | 3 | |
| 4 | F2 | 4 | 6.17±0.06 |
| 5 | | 5 | |
| 6 | | 6 | |
| 7 | F3 | 7 | 6.30±0.10 |
| 8 | | 8 | |
| 9 | | 9 | |

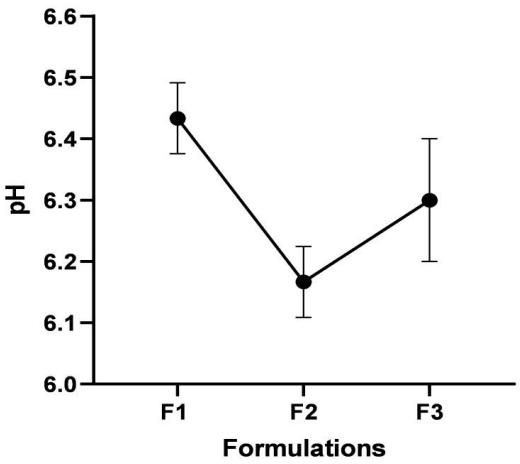



**Fig.1- pH of Nanoemulgel**

#### 1.4.3. Extrudability [27]

Extrudability was examined why the aluminum collapsible tubes. The formulation was filled completely into the aluminum collapsible tubes. The tube had applied pressure of about 500g and the extruded amount was measured. Approximately 0.2 meter per second ribbon of the formulation should be expelled from the aluminum collapsible tubes. If the amount is exceeded from 0.2 meter per second then the formulation is considered to be excellent.

**Extrudability=Applied weight to extrude gel from tube (g)/ area (cm2)**

**Table-5: Extrudability of Nanoemulgel**

| S.no | Extrudability |
|---|---|
| **F1** | Good |
| **F2** | Excellent |
| **F3** | Good |

### 1.4.4. Spreadability [28]

This parameter has been evaluated by utilizing the spreadability equipment, which is formed of a plank of wood including a scale and two glass slides, the spreadability of the transdermal preparations has been examined.

Spreadability was evaluated to examine the spreading ability of the formulated nanoemulgel when applied to the skin. Spreadability was assessed with using the sandwich method, in this method two glass plates were used the first class plate which was already pre marked at 15 CM diameter. The Other glass plate which was not marked. The formulation was placed over the first glass plate and the other glass plate was put over the first glass plate. Approximately 500 grams were placed over the glass plates so that force applied between the formulations. The circle of spread was calculated and recorded in table-8.

**Table-6: Spreadability of Nanoemulgel (Mean ± SD)**

| Sn. | Formulations | Triplicates | Spreadability(cm/sec) (Mean ± SD) |
|---|---|---|---|
| 1 | F1 | 1 | 11.01±0.40 |
| 2 | | 2 | |
| 3 | | 3 | |
| 4 | F2 | 4 | 11.90±0.56 |
| 5 | | 5 | |
| 6 | | 6 | |
| 7 | F3 | 7 | 11.77±0.44 |
| 8 | | 8 | |
| 9 | | 9 | |

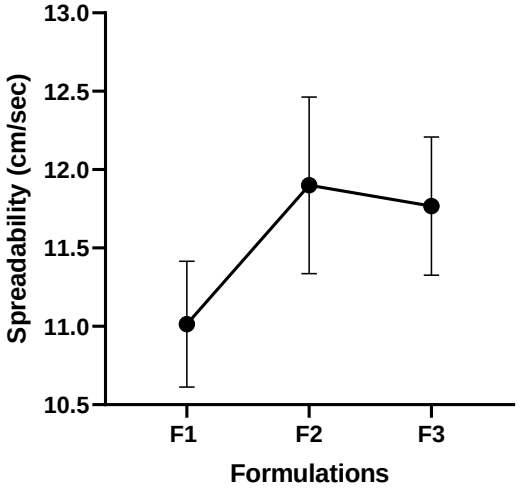



**Fig.2- Spreadability of Nanoemulgel**

### 1.4.5. Viscosity [29]

Viscosity was identified using the digital viscometer (IGene Labserve-100) at three different RPM 40 and 50 with the spindle number 3. The 100 mL of the sample was taken in the glass beaker and placed under the probe of the digital viscometer until the probe touches to the beaker surface. The reading was noted down once the digital display fluctuation stops and recorded. The viscosity denotes the interaction between the polymers and the excipients. The viscosity was also performed three times for each formulation. The viscosity was recorded in table-9.

**Table-7: Viscosity of Nanoemulgel (Mean ± SD)**

| Sn. | Formulations | Triplicates | Viscosity (cps) | |
|---|---|---|---|---|
| | | | 40 RPM | 50 RPM |
| 1 | F1 | 1 | 12002.33±12.06 | 10919.33±81.10 |
| 2 | | 2 | | |
| 3 | | 3 | | |
| 4 | F2 | 4 | 12084.33±34.59 | 11297.67±60.74 |
| 5 | | 5 | | |
| 6 | | 6 | | |
| 7 | F3 | 7 | 11992.33±31.88 | 10888.00±95.60 |
| 8 | | 8 | | |
| 9 | | 9 | | |

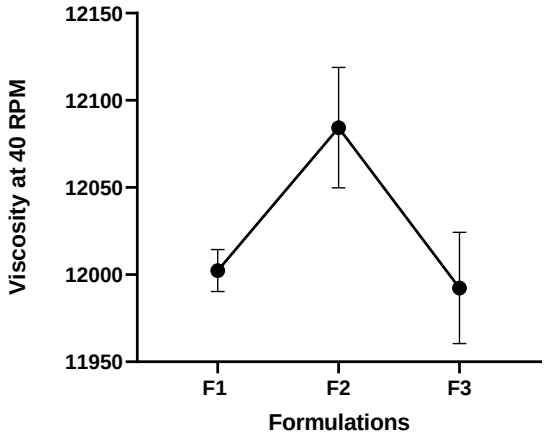



**Fig.3- Viscosity at 40 RPM**

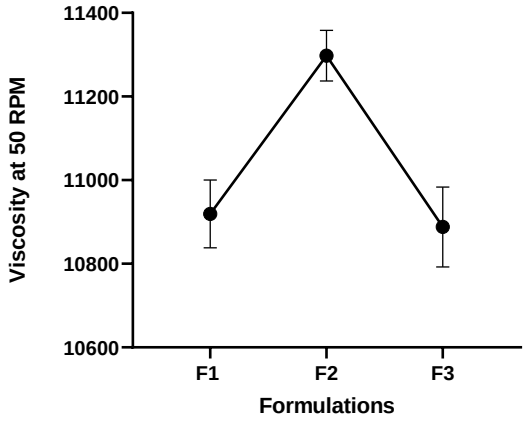



**Fig.4- Viscosity at 50 RPM**

### 1.4.6. In vitro Drug Release [30]

In vitro drug release study was carried out to examine the release through the skin basically mimic the activity of the skin. The Franz diffusion cell apparatus was used in this experiment. The 1g of drug was placed on the dialysis membrane and eventually penetrates through the dialysis membrane when it comes in contact with the phosphate buffered saline (7.4 pH at 37±1°C). The experiment was performed for 8 hours to observe the percentage drug release. Each hour the 1 ml of sample was taken and analyzed by the Ultraviolet Visible Spectrophotometry at 315 NM.

**Table-8: Viscosity of Nanoemulgel (Mean ± SD)**

| Sn. | Time | F1 | F2 | F3 |
|---|---|---|---|---|
| 1 | 0 | 0 | 0 | 0 |
| 2 | 1 | 11.01±0.3 | 10.25±0.4 | 12.24±0.1 |
| 3 | 2 | 28.21±0.2 | 30.11±1.0 | 27.25±0.5 |
| 4 | 3 | 35.02±0.3 | 39.25±0.7 | 30.28±0.4 |
| 5 | 4 | 51.27±0.3 | 59.82±1.0 | 50.13±0.9 |
| 6 | 5 | 59.88±0.2 | 61.34±0.1 | 60.89±0.5 |
| 7 | 6 | 62.41±0.7 | 72.98±0.8 | 68.32±0.5 |
| 8 | 7 | 78.96±0.03 | 85.25±0.5 | 78.32±0.9 |
| 9 | 8 | 90.00±0.5 | 95.66±0.3 | 89.69±0.2 |

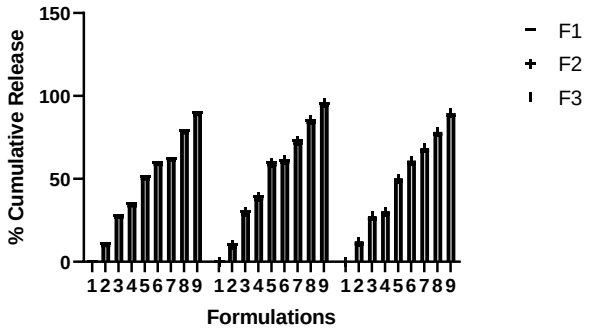



**Fig.5- In vitro Drug Release**

### 1.4.7. Determination of Particle Size, and Zeta Potential

**Particle Size [31]**

Particle size of the prepared herbal Nanoemulgel was assessed using the technology dynamic light scattering method (ZS 90, Malvern Instrument Ltd, UK). The particle size of nanoemulgel is one of the most important characteristics that determine its physical and chemical properties. It also affects the stability, usability, and efficacy of the formulation. The mean particle size (MPS) of nanoemulgel should be less than 200 nm for dermal application. The formulated Nanoemulgel was diluted with the deionized water at the ratio of 1:1000 and the particle size was examined (table-11).

**Zeta Potential [31]**

Zeta potential is a measure of the electrostatic repulsion between particles in a suspension. If the repulsion is strong, the particles will be less likely to stick together or settle out of suspension. Nanoemulgel typically have high

zeta potentials because the nanoparticles are electrically charged. The zeta potential of nanoemulgel was measured to be >-37.40 mV. This value is within the range of values that are typically considered to be stable. A lower zeta potential indicates a more stable system. Zeta potential for nanoemulgel was estimated using Zeta sizer (ZS 90, Malvern Instrument Inc, UK) by using an electrophoretic light scattering method

**Table-9: Zeta Potential, Particle Size and Polydispersity Index of Nanoemulgel (Mean ± SD)**



| Sn. | Formulations | Triplicates | Zeta Potential | Particle Size | Polydispersity Index |
|---|---|---|---|---|---|
| 1 | F1 | 1 | 37.40±0.44 | 101.18±0.07 | 0.7 |
| 2 | | 2 | | | |
| 3 | | 3 | | | |
| 4 | F2 | 4 | 24.60±0.44 | 100.22±0.16 | 0.5 |
| 5 | | 5 | | | |
| 6 | | 6 | | | |
| 7 | F3 | 7 | 30.83±0.55 | 102.20±0.10 | 0.6 |
| 8 | | 8 | | | |
| 9 | | 9 | | | |

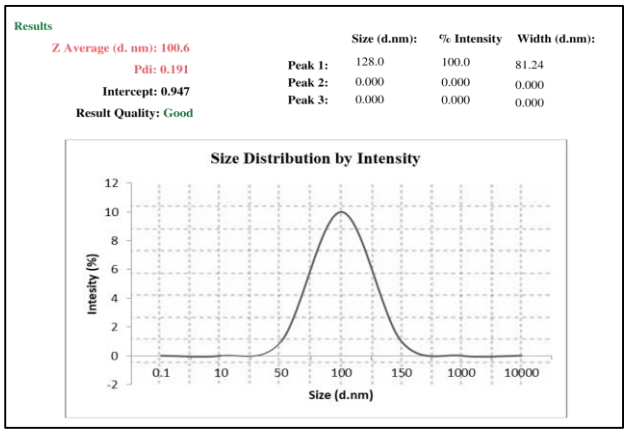



**Fig.6- Particle Size**

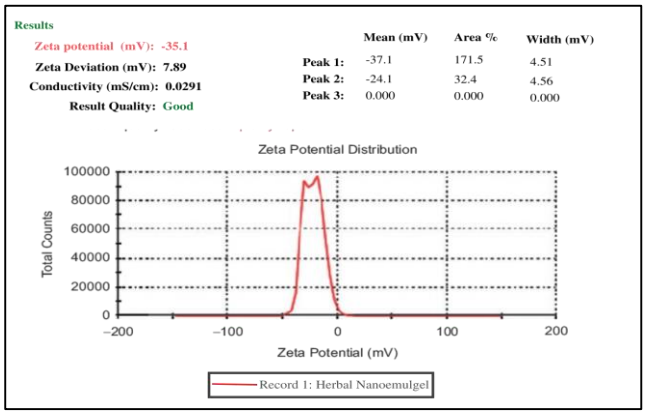



**Fig.7- Zeta Potential**

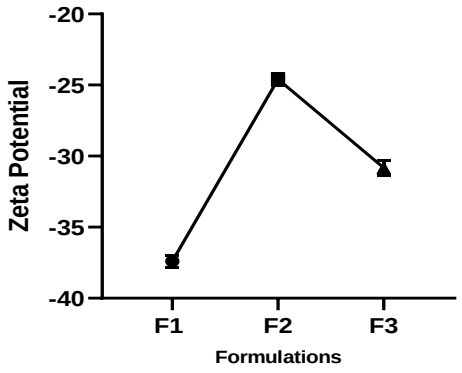



**Fig.8- Zeta Potential**

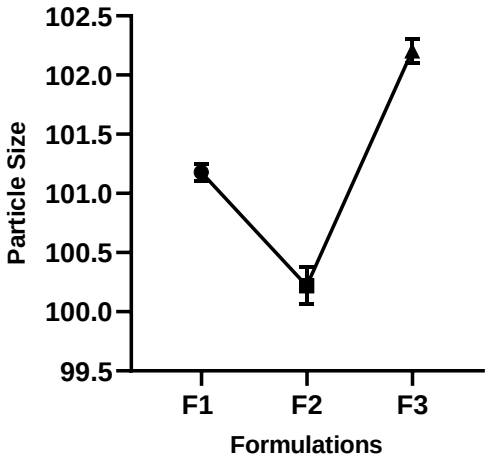



**Fig.9- Particle Size**

## 3.0 In vitro Cytotoxicity Assay [32]

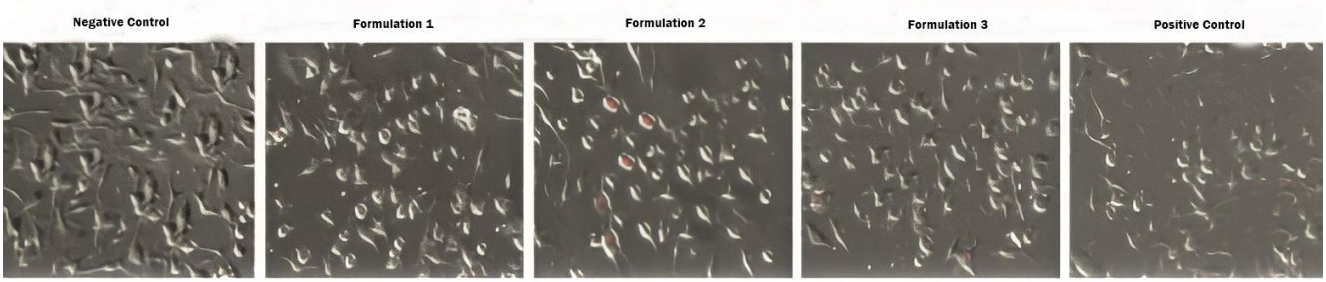
### 3.1. Procedure

**Formulation 1, 2 &3 for both the cell lines (RAW 264.7)**

The cell line was grown up in the Dulbecco's Modified Eagle's Medium (DMEM) for 24h at 5% $CO_2$ at 37°C with >90% humidity. After 48h, the cell lines were checked for the confluency and appearance. Cell lines was transferred in the 96 well plates, and exposed the 100µl of test item, positive control, negative control and blank was added in duplicates into the respective wells. Total 8 different concentrations (0.039 mg/mL, 0.078 mg/mL, 0.156 mg/mL, 0.312 mg/mL, 0.625 mg/mL, 1.25mg/mL, 2.5mg/mL and 5 mg/mL) of the test item were added and the concentration of the positive control was 5 mg/mL. The cells were further incubated in Dulbecco's Modified Eagle's Medium (DMEM) for 24h at 5% $CO_2$ at 37°C with >90% humidity.

**Observation**

For both the cell lines exposure, after 24h treatment, cells were examined using phase contrast microscope to check the morphological changes. After incubation for 24 hours, the media was removed and replaced with fresh media containing MTT solution (5 mg/mL). The plate was then incubated for an additional 4 hours. At the end of the incubation period, the media was removed and replaced with fresh media. The plates were then placed in a micro plate reader and absorbance was measured at 570 nm wavelength. The colour shift to yellow is acidic pH and the colour shift to magenta to purple is alkaline pH. Absorbance was measured at 550nm using Biorad Micro plate reader to ensure the cell viability.



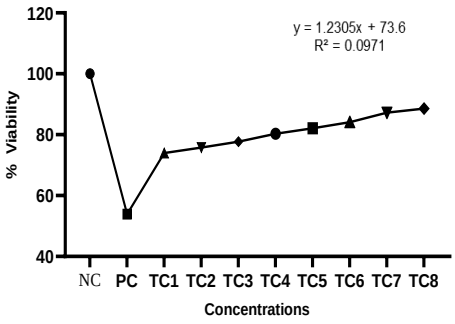




**Fig.10- OD vs. %Viability for Formulation 1**

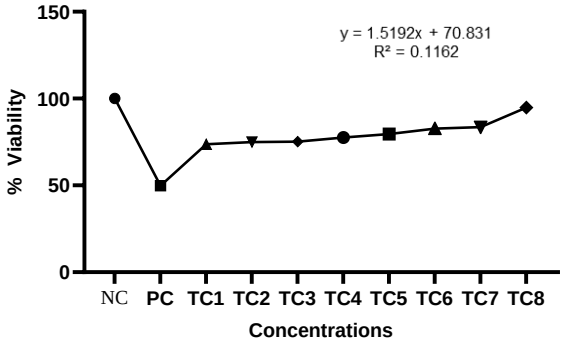



**Fig.12- OD vs. %Viability for Formulation 3**

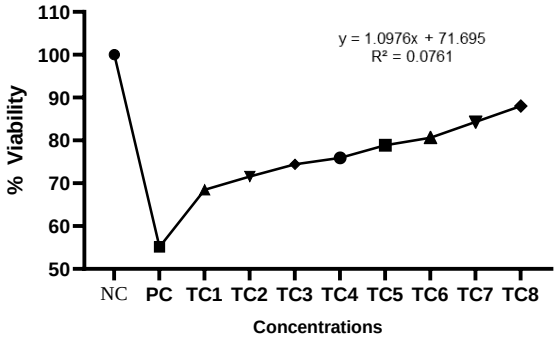



**Fig.11- OD vs. %Viability for Formulation 2**

## 4.0 In Vitro Anti-Inflammatory Assay [33]

### IL6 release in RAW264.7

After growing up (70-80% confluency) the cells was removed from culture flasks by enzymatic digestion (Trypsin/EDTA) and the cell suspension was centrifuged (1100-1200 rpm for 10 min). The cells were re-suspended in culture medium at a density of 1-3 x $10^5$cells/mL. Plate

map (96-well micro titre plate) was prepared for blank, negative control and for test item.

### Test item exposure

After 24h of incubation, 100□l of test item at eight concentration (5mg/mL) with LPS (1mg/mL), positive control (LPS, 5mg/ml), negative control (cell alone) and blank (media only) were added in duplicates into the respective wells of the 96-well plate. The cells were further incubated for 24h at 5% CO2 at 37°C with >90% humidity.

After 24 hours, the content in each well were transferred to the individually labelled 2ml centrifuge vials. The contents were centrifuged at 1100 rpm for 5 minutes. Then the cell culture supernates were collected in a fresh labelled eppendorf tubes and stored in refrigerator (2-8 °C) for the estimation of level of IL-6 released using ELISA Kit procured from BOSTER; Human IL-6, ELISA Research Reagent was used for the IL-6 measurement as per ELISA manual. The assay samples were kept in 2-8°C till analysis.

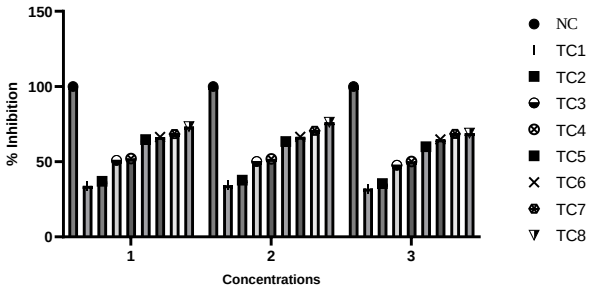



**Fig.13- Formulations vs. % Inhibition**

## 5.0 Results and Discussion

The Nanoemulgel of Aloe Vera and Nyctanthes Arbor leaves extract was successfully formulated and characterized. The nanoemulgel was prepared using a self-Nano emulsifying drug delivery system approach, and the physical stability, in vitro skin permeation, and in vitro anti-inflammatory activity were evaluated. Transdermal absorption enhancement strategies like penetration enhancers can be used for better skin permeation but they may cause irritation or other side effects [36]. Hence, there is a need to develop new formulations like nanoemulgel which can improve the skin permeation of Aloe Vera and Nyctanthes Arbor leaves extract without causing any side effects [37].

The results showed that the nanoemulgel had good physical stability with no significant change in size or particle distribution over time. The in vitro skin permeation studies revealed that the nanoemulgel significantly increased the penetration of Aloe Vera and Nyctanthes Arbor leaves extract through the skin compared to the cream formulation. The results of in vitro release study showed that the formulation exhibited a controlled release profile over a period of 8 h. The mean particle size, zeta potential, and viscosity of nanoemulgel were found to be 100.22±0.16 to 102.20±0.10, 24.60±0.44 to 37.40±0.44, 11992.33±31.88 to 12084.33±34.59 at 40 RPM and 10888.00±95.60 to 11297.67±60.74 at 50 RPM respectively which indicated successful development of stable nanoemulgel formulation.



Finally, the in vivo anti-inflammatory activity and cytotoxicity potential of the nanoemulgel was assessed using an in vitro IL-6 inhibition (76.22 % in formulation 2) model using RAW 264.7 cell lines. Treatment with the Aloe Vera and Nyctanthes Arbor leaves extract nanoemulgel resulted in a significant increase in % inhibition of the IL6 and no cytotoxicity was observed during the experiment, indicating enhanced efficacy due to improved topical delivery. These results demonstrate that SNEDDS-based formulations can be used to improve topical drug delivery and efficacy of herbal extracts such as Aloe Vera and Nyctanthes Arbor leaves extract.

The results showed that the nanoemulgel had a lower viscosity, smaller particle size and higher zeta potential than the control gel [38]. These results indicate that the nanoemulgel formulation has better physical stability and can be easily applied to the skin. The zeta potential of the nanoemulgel was also found to be negative, which indicates that it has good skin compatibility [39].

The findings of this study suggest that the herbal Nanoemulgel could be a promising natural therapy for treating inflammation. Further studies are warranted to elucidate the mechanisms underlying the therapeutic effects of this formulation.

## 6.0 Conclusion

The Nanoemulgel of Aloe Vera and Nyctanthes Arbor leaves extract was successfully prepared and characterized. The formulation showed potential to be used as effective topical drug delivery system for anti-inflammatory activity of Aloe Vera and Nyctanthes Arbor leaves with Carbapol 934.The study concludes that the herbal nanoemulgel of Aloe Vera and Nyctanthes Arbor leaves is a successful topical drug delivery system. This formulation can be used to effectively treat inflammation.

## 7.0 REFRENCES

1. Reddi, D., Curran, N., & Stephens, R. An introduction to pain pathways and mechanisms. British Journal of Hospital Medicine,2013; 74(Sup12), C188–C191
2. International Association for the Study of Pain. IASP Terminology. 2020
3. Moayedi M, Davis KD. Theories of pain: From specificity to gate control. J Neurophysiol 2013;109:5-12.
4. Świeboda P, Filip R, Prystupa A, Drozd M. Assessment of pain: types, mechanism and treatment. Pain. 2013;2(7).
5. Astuti K. W, Wijayanti N. P. A. D, Yustiantara P. S, Laksana K. P, Putra P. S. A. Anti-Inflammatory Activity of Mangosteen (Garcinia Mangostana Linn.) Rind Extract Nanoemulgel and Gel Dosage Forms. Biomed Pharmacol J 2019;12(4).
6. Abdallah, M. H., Abu Lila, A. S., Unissa, R., Elsewedy, H. S., Elghamry, H. A., & Soliman, M. S. (2021). Preparation, characterization and evaluation of anti-inflammatory and anti-nociceptive effects of brucine-loaded nanoemulgel. Colloids and Surfaces B: Biointerfaces, 205
7. P. van Hoogevest, X. Liu, A. Fahr, Drug delivery strategies for poorly water-soluble drugs: the industrial perspective, Expert Opin. Drug Deliv. 8 (2011) 1481–1500.
8. M.C. Pena-Juarez, O.R. Guadarrama-Escobar, J.J. Escobar-Chavez, Transdermal delivery systems for biomolecules, J. Pharm. Innov. (2021).
9. M. Isaac, C. Holvey, Transdermal patches: the emerging mode of drug delivery system in psychiatry, Ther. Adv. Psychopharmacol. 2 (2012) 255–263.
10. K.S. Paudel, M. Milewski, C.L. Swadley, N.K. Brogden, P. Ghosh, A.L. Stinchcomb, Challenges and opportunities in dermal/transdermal delivery, Ther. Deliv. 1 (2010) 109–131.
11. Eid AM, El-Enshasy HA, Aziz R, Elmarzugi NA (2014) Preparation, Characterization and Anti-Infammatory Activity of Swietenia macrophylla Nanoemulgel. Journal of Nanomedicine Nanotechnology, Vol. 5: Pgno.190
12. Chen H, Khemtong C, Yang X, Chang X, Gao J. Nanonization strategies for poorly water-soluble drugs. Drug Discov Today. 2011 Apr;16(7-8):354-60.
13. Shakeel F, Ramadan W, Ahmed MA. Investigation of true nanoemulsions for transdermal potential of indomethacin: characterization, rheological characteristics, and ex vivo skin permeation studies. J Drug Target. 2009 Jul;17(6):435-41
14. Ajazuddin, Alexander A, Khichariya A, Gupta S, Patel RJ, Giri TK, Tripathi DK. Recent expansions in an emergent novel drug delivery technology: Emulgel. J Control Release. 2013 Oct 28;171(2):122-32.
15. Ishan Ghai, Hema Chaudhary, Shashank Ghai, Kanchan Kohli and Vikash Kr, A Review of Transdermal Drug Delivery Using Nano-Vesicular Carriers: Transfersomes; Bentham Science, Vol. 2, isuue.2; 2012, Pgno. 164-171
16. R.M. Aman, H. Abu II, M.M. Meshali, Novel clove essential oil nanoemulgel tailored by Taguchi's model and scaffold-based nanofibers: phytopharmaceuticals with promising potential as cyclooxygenase-2 inhibitors in external inflammation, Int. J. Nanomed. 15 (2020) 2171–2195.
17. M.K. Jeengar, S.V. Rompicharla, S. Shrivastava, N. Chella, N.R. Shastri, V.G. Naidu, R. Sistla, Emu oil based nano-emulgel for topical delivery of curcumin, Int. J. Pharm. 506 (2016) 222–236.
18. M. Rahil G. Bhura, Khushboo A. Bhagat and Samir K. Shah, Formulation and evaluation of topical nano emulgel of adapalene, World Journal of Pharmaceutical Sciences, 2015; Vol.3 ; Pgno. 1013-1024
19. Abdallah, M. H., Abu Lila, A. S., Unissa, R., Elsewedy, H. S., Elghamry, H. A., & Soliman, M. S. (2021). Preparation, characterization and evaluation of anti-inflammatory and anti-

nociceptive effects of brucine-loaded nanoemulgel. Colloids and Surfaces B: Biointerfaces, 205, Pgno. 1128-1135

20. Sheela A Yadav1, Sushilkumar S Poddar, Formulation, In-Vitro And In-Vivo Evaluation of Nanoemulsion Gel For Transdermal Drug Delivery Of Nimodipine, Asian J Pharm Clin Res, Vol 8, 2015, Pgno. 119-124

21. Ahmad M Eid, Hesham A El-Enshasy, Ramlan Aziz and Nagib A Elmarzugi, Preparation, Characterization and Anti-Inflammatory Activity of Swieteniamacrophylla Nanoemulgel, Nanomedicine and Nanotechnology, 2014, Vol. 5; Pgno.2-8.

22. Morsy, M. A., Abdel-Latif, R. G., Nair, A. B., Venugopala, K. N., Ahmed, A. F., Elsewedy, H. S., & Shehata, T. M. (2019). Preparation and evaluation of atorvastatin-loaded nanoemulgel on wound-healing efficacy. Pharmaceutics, 11(11), 609.

23. Soliman, W. E., Shehata, T. M., Mohamed, M. E., Younis, N. S., & Elsewedy, H. S. (2021). Enhancement of curcumin anti-inflammatory effect via formulation into myrrh oil-based nanoemulgel. Polymers, 13(4), 577.

24. Nagaraja, S., Basavarajappa, G. M., Attimarad, M., & Pund, S. (2021). Topical Nanoemulgel for the Treatment of Skin Cancer: Proof-of-Technology. Pharmaceutics, 13(6), 902.

25. Abdallah, M. H., Lila, A. S. A., Unissa, R., Elsewedy, H. S., Elghamry, H. A., & Soliman, M. S. (2021). Preparation, characterization and evaluation of anti-inflammatory and anti-nociceptive effects of brucine-loaded nanoemulgel. Colloids and Surfaces B: Biointerfaces, 205, 111868.

26. Soliman, W. E., Shehata, T. M., Mohamed, M. E., Younis, N. S., & Elsewedy, H. S. (2021). Enhancement of curcumin anti-inflammatory effect via formulation into myrrh oil-based nanoemulgel. Polymers, 13(4), 577.

27. Tungadi, R., & Wicita, P. (2020). Formulation, optimization, and characterization of snakehead fish (Ophiocephalus Striatus) powder nanoemulgel. Brazilian Journal of Pharmaceutical Sciences, 56.

28. Ting, T. C., Abdullah, N. H., Ramle, S. F. M., Sofi, A. Z. M., & Zaudin, N. A. C. (2022, June). Development of Piper betle nanoemulgel formulation for effective droplet size reduction and excellent stability. In AIP Conference Proceedings (Vol. 2454, No. 1, p. 060017). AIP Publishing LLC.

29. DAS, S., Sharadha, M., Venkatesh, M. P., SAHOO, S., TRIPATHY, J., & Gowda, D. V. (2021). Formulation and evaluation of topical nanoemulgel of methotrexate for rheumatoid arthritis. International Journal of Applied Pharmaceutics, 351-357.

30. Nikam, M., Yendapalli, P., Ravichandra, V. D., & Pai, V. FORMULATION AND EVALUATION OF TOPICAL NANOEMULGEL OF MORINGA OLEIFERA LEAVES EXTRACT.

31. Eid, A. M., Istateyeh, I., Salhi, N., & Istateyeh, T. (2019). Antibacterial activity of Fusidic acid and sodium Fusidate nanoparticles incorporated in pine oil Nanoemulgel. International Journal of Nanomedicine, 14, 9411.

32. Gadhave, D., Rasal, N., Sonawane, R., Sekar, M., & Kokare, C. (2021). Nose-to-brain delivery of teriflunomide-loaded lipid-based carbopol-gellan gum nanogel for glioma: Pharmacological and in vitro cytotoxicity studies. International Journal of Biological Macromolecules, 167, 906-920.

33. Yeo, J., Lee, J., Yoon, S., & Kim, W. J. (2020). Tannic acid-based nanogel as an efficient anti-inflammatory agent. Biomaterials science, 8(4), 1148-1159.