Formulation and Evaluation of Anti inflammatory Gel Containing Herbal Extract Nyctantus Arbor Tritis

Sayali Hogade[1], Akshada Deshmukh[2], Shivtej Patil[3], Riya Patil[4], Prajkta Patil[5], Sanjana Patil[6], Pratiksha Patil[7]

[1,2,3,4,5,6,7]*Ashokrao Mane College of Pharmacy, Peth-Vadgaon*

Abstract—Herbal medicines is still the mainstay of about 75-80% of the world's population, mainly in developing countries, for primary health care because of better cultural acceptability, better compatibility with human body and lesser side effects. Herbal medicines consist of plant or its part to treat injuries, disease or illnesses and are used to prevent and treat diseases and ailments or to promote health and healing. It is a drug or preparation made from a plant or plants and used for any to such purpose. Herbal medicines are the oldest form of health care known to mankind. Gel formulations prepared with Carbopol 934 showed good homogeneity, no skin irritation, good stability and anti-inflammatory activity. However, the Xanthan gum based gel proved to the formula of choice, since it showed the highest percentage of extrudability, good spreadability and rheological properties. Formulation F2 and F3 showed the best formulation with significant anti-inflammatory activity. Formulation F1 shows approximately equal anti-inflammatory activity.

Index Terms –Herbal ingredient, Evalution, Formulation.

INTRODUCTION-

Inflammation is latin word which means part of the complex biological response of body tissues to the harmful stimuli, such as pathogens, damaged cells, or irritants & is protective response involving immune cells, blood vessels & molecular mediators. It is the dynamic response of vascularized tissue to injury. The unique feature of the inflammatory process is the reaction of blood vessel leading to the accumulation of fluid and leucocytes in the extra vascular tissue.

Signs of Inflammation

- Rubor : Redness
- Calor : Warmth / Heat
- Dolor : Pain
- Tumor : Swelling
- Loss of function

Causes of Inflammation

- Physical Agents: Mechanical injuries, alteration in temperatures & pressure, radiation injuries.
- Chemical Agents: It includes increasing list of drugs & toxins.
- Biological Agents: Bacteria, viruses, fungi, parasites.
- Immunological Disorders: Hypersensitivity reactions, autoimmunity, immuno deficiency status, etc.
- Genetic/ Metabolic Disorders: Gout, diabetes mellitus

Types of Inflammation

1. Acute Inflammation
2. Chronic Inflammation

Acute Inflammation: it is short duration and it represents the early body reaction and it is usually followed by repair. The main features of acute inflammation are as follows.

- Accumulation of fluid and plasma at the affected site.
- Intravascular activation of platelets.
- Polymorphonuclear neutrophils as inflammatory cells.

Chronic Inflammation: It is longer duration & it occurs either after the causative agent of Acute Inflammation persists for longer time or stimulus is such that it reduces chronic inflammation from the beginning. The main features of chronic Inflammation is presence of chronic inflammatory cells such as lymphocytes, plasma cells, & macrophages.

Gels

Gels are homogeneous, semi-solid preparations used to cure and prevent skin Conditions. Due to the

hydrophilic nature of gels, the medicine or active component was released quickly. A gel is made up of two parts: a cross-linked, three-dimensional substance That contains a significant volume of liquid to create a sufficient, stiff network that Immobilizes the liquid continuous phase. Both organic macromolecules and inorganic Particles are employed to create the structural network of gel. Chemical gels have a Permanent covalent bonding that binds the particles together, whereas physical topical gels Have secondary intermolecular forces includes hydrogen bonds, electrostatic interactions, Hydrophobic contacts, and Vander Waal forces that are weaker and reversible.

IDEAL PROPERTIES OF TOPICAL GEL

- The gel should be clear and homogenous.
- The gel should be inert in nature.
- The gel should be non-sticky.
- The gel should not interact with any other formulation component.
- The gel should be stable.
- It should be non-irritate to the skin or any part where the gel is applied.
- The viscosity is should be optimum.
- It should have anti- microbial activity.

ADVANTAGES OF GEL FORMULATIONS

Some main advantages of gel formulation over other semisolid dosage forms.

- Gels are effortless to prepare when compared to other formulations.
- Gel is elegant non-greasy formulation.
- Gels have excellent adherence property to application site.
- Gels are biocompatible and eco-friendly.
- Have magnificent tolerability to stress conditions

Properties of Gel

Hydration: Water can be added to renew an elastic gel that has fully lost all of its moisture. However, once a nonelastic gel is dry, adding more water won't cause it to gel.

Swelling: Elastic gels that have been partially dehydrated absorb water when immersed in the solvent. This results in an increase in the gel's volume, a process known as swelling.

Syneresis: On standing, many inorganic gels shrink, and this shrinkage is often accompanied by solvent exudation. This process is called syneresis.

Thixotropy: When at rest, some gels are semisolid; yet, when disturbed, they become liquid sol. This reversible sol-gel transformation is referred to as Thixotropy. Gels made of iron oxide and silver oxide exhibit this characteristic.

CLASSIFICATION OF GELS

Gels can be classified based on colloidal phases, nature of solvent used, physical nature and Rheological properties

Based on colloidal phases: They are classified into:

- Inorganic (Two phase system)
- Organic (Single phase system)

Inorganic (Two-Phase System) : The system consist of floccules of tiny particles rather than larger molecules and the gel Structure will be unstable if the dispersed phase partition size is especially large and develops a three-dimensional structure throughout the gel. They must be thixotropic, which means that when disturbed, they transform from a semisolid to a liquid. Gel made of aluminium Hydroxide and bentonite magma are two examples.

Organic (Single Phase System)

On the twisted threads, there are large organic molecules that are continuously dissolved. The Majority of organic gels are single-phase solutions made up of organic liquids such Plastic Base and gelling agents like carbomer and tragacanthin.

Based on Nature of the Solvent

- Hydrogels: (water based):A hydrogel is a three-dimensional network of hydrophilic polymers that can grows in water And contain a significant quantity of water while maintaining their structural integrity due to The chemical or physical cross-linking of individual polymer chains. Hydrophilic colloids like Silica, bentonite,

tragacanth, pectin, sodium alginate, etc. provide an example. The hydrogel May be utilised as an ECG medical electrode, rectal medication delivery system, and Sustained release drug delivery system.

- Organogel: (With a non-aqueous solvent): A liquid organic phase is contained within a Three-dimensional, cross-linked network in an organogel, a type of gel. The addition of a Polar solvent causes the organogelling or gelation of lecithin solution in organic solvents.
- Xerogels: Xerogels are solid-formed gels created by allowing materials to gently dry at room Temperature while experiencing unrestricted shrinking. Viscous sintering takes place when a Xerogel is heated over a certain point, thereby turning the porous gel into a thick glass. Examples include polystyrene, dry cellulose, and tragacanth ribbons.

Gels are occasionally Categorized as plastic gels, pseudo-plastic gels, and thixotropic gels because they display Non-Newtonian flow.

Based on Physical Nature

- Elastic gels: Agar, pectin, Guar gum, and alginates gels have an elastic property. At the point of junction, the fibrous molecules are joined by comparably weak connections such as Hydrogen bonds and dipole attraction. If the molecule has a free -COOH group, a salt bridge of the type -COO-X-COO forms an extra bond between two adjacent strand networks. Eg.: Alginate and Carbopol.
- Rigid gels: This can be made from macromolecules with primary valence bonds connecting the framework. Eg. Silic acid molecules are kept together in a silica gel by the Si-O-Si-O Link, resulting in a polymer structure with a network of pores.

GELLING AGENT: Gelling agents are the polymers that are used to structural network or provide texture to the Gels. Gelling agents are classified as follows: Polymers are used to give the structural network, which is essential for the preparation of Gels. Gel forming Polymers are classified as follows:

1. Natural Polymers:

Proteins – Collagen, Gelatin

Polysaccharides – Agar, Alginate acid Sodium or Potassium carageenan, Tragacanth, Pectin, Guar Gum, Cassia Tora, Xanthan, Gellum Gum.

2. Semisynthetic polymers cellulose derivatives: Carboxymethyl cellulose, Methylcellulose, Hydroxyethyl cellulose Hydroxypropyl cellulose, Hydroxy propyl (methyl cellulose).
3. Synthetic polymers: Carbomer – Carbopol 940, Carbopol 934, Polyacrylamide Poloxamer, Polyvinyl Alcohol, Polyethylene and its copolymers.
4. Inorganic substances: Bentonite Aluminum hydroxide
5. Surfactants: Cebrostearyl alcohol, Brij – 96

Plant Material : Nyctantus Arbor Tritis

Nyctanthus arbor-tristis Linn. (Oleaceae) is popularly known as ‘Night Jasmine’ or ‘Harsinghar’ (Hindi) due to the fact that is flowers emit a very strong and pleasant fragrance during the whole night Nyctanthus is commonly known as: a. Night flowering jasmine b. Coral jasmine c. Parijat in Hindi Virtually all parts of the plant have been used in different diseases and in different indications. By and large, different parts have following activities like:

a. Leaves – antibacterial, anti-inflammatory, anti-fungal, anti-pyretic

b. Flowers – anti-filarial, antioxidant, diuretic

c. Seeds – antifungal, antibacterial, antileishmanial, immunomodulatory

d. Stem – antipyretic and antioxidant e. Bark – anti-microbial f. Flower oil – as perfume

Materials

Sr.no	Ingredients	Manufacturing company
1	Carbopol 934	LOBACHEMICALPVTLTD
2	Polyethylene glycol	MOLYCHEM MUMBAI
3	Propyl paraben	SD LAB PVT LTD
4	Methyl paraben	SD LAB PVT LTD
5	Menthol oil	MOLYCHEM MUMBAI
6	Triethanolamine	MOLYCHEM MUMBAI

Table No.1

METHODS OF EXTRACTION

Leaves of Nyctantus Arbor Tritis was cleaned & take in a beaker containing 100 ml of water. Simply decoction method is used for the Extraction process.

The heating is done for at least 1 hour with continuous stirring. After one hour the extract of drug was cooled at room temperature and filtered out.

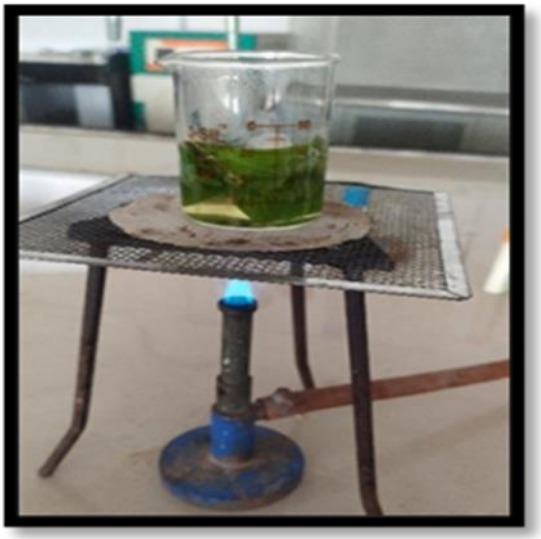

Fig No. 1

Preparation of Anti-Inflammatory Gel :
The gel was prepared in two steps;
Step 1: The required weight quantity of Carbopol 940 was added to a 50 mL of warm water and was mixed continuously on hot water plate to maintain the temperature at 40°C.
Step 2: In another beaker extract of drug was taken, to this propylene glycol was added.Then the contents were transferred to the carbopol mixture and finally preservatives methyl paraben and Propyl paraben were added and mixed thoroughly to make 100mL.

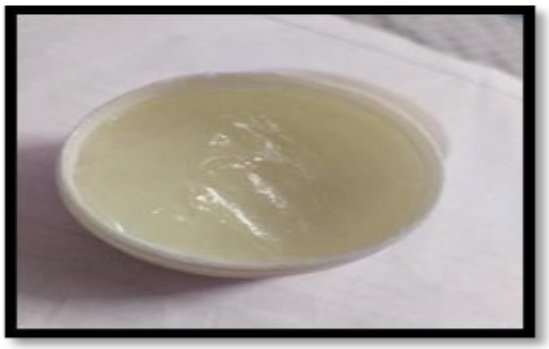

Fig.No.2

Triethanolamine was added to maintain the pH at 7 and menthol oil was added and gel was preapared by using magnetic stirrer. Stirring was done until we get the gel consistency. Similarly, the formulations 1 to 3 were prepared.

Formulation Table :

Ingredients	F1	F2	F3
Herb extract	4	4	4
Carbopol 934	0.5	1.0	1.5
Propylene glycol	10	10	10
Propyl paraben	0.5	0.5	0.5
Methyl paraben	0.2	0.2	0.2
Triethanolamine (q.s)	q.s	q.s	q.s
Menthol oil	0.1	0.1	0.1
Purified water(q.s)	q.s	qs	q.s

Table No.2

Evaluation of Anti-inflammatory Gel :
Rheological Characteristic: For anti inflammatory gel compositions, the rheological Characteristic was examined (colour, clogging, homogeneity and texture).

Washability: After applying the formulations to the skin, the ease and extent of washing with water were personally assessed.

Spreadability: gels must have good spreadability, which is a crucial criterion. Spreadability is a phrase used to describe the area across which the gel spreads easily when applied to hairs. A formulation's medicinal efficacy is also influenced by its spreading value. To investigate the spreadability of the formulations, specific equipment was created. Spreadability is measured by the time it takes two slides to slip away from a formulation when they are put between each other and subjected to a specific load. The spreadability improves as the time it takes to separate two slides decreases. Two standard-sized glass slides (6×2) were selected. One of the slides was covered with the hair gel formulation whose spreadability was to be determined. The hair gel mixture between the two slides was traced uniformly to form a thin layer by placing 100 grams of weight on the upper slide. The extra hair gel formulation sticking to the slides was scraped off and the weight was eliminated. The bottom slide was attached to the apparatus's board, and one end of the higher slide was tied to a string to which a 20-gram load could be imparted using a simple pulley. The time it took for the upper slide to travel 6 cm and separate from the lower slide under the weight's direction was recorded. The experiment was done six times, with the average of the results. Spreadability = m*l/t

Where,
S=Spreadability (gcm/sec)
m = weight tied to the upper slide (20 grams)
l = length of glass slide (6cms).
T = time taken is seconds.

Determination of pH: A digital pH meter was used to determine the pH of the gels. One gram of gel was dissolved in 25 ml of distilled water, and the electrode was immersed in the solution for 30 minutes until a steady reading was obtained. It was also stated that she was always reading. The pH measurements of each formulation were double-checked.

Determination of Viscosity :A Brookfield digital viscometer was used to measure the viscosity of the produced gel. The viscosity was determined using spindle no. 64 at 10 rpm and 25°C. A adequate amount of gel was dispensed into a wide mouth container. The gel was placed in the wide mouth container in such a way that it would allow the Viscometer's spindle to be dipped. Before the measurements, the gel samples were allowed to settle for 30 minutes at a constant temperature (25±/1°C).

Drug content :
Procedure:
In a UV visible spectrophotometer with a 1 cm pathlength and a wavelength of 296 nm, measure the absorbance of both the standard and sample solution against a blank and calculate the concentration of using the formula below.
Drug Content –absorbance of test /absorbance of standard drug × 100

In-vitro Drug Release Studies Using the Franz Diffusion Cell
Diffusion Studies:
Preparation of Phosphate Buffer pH 7.4: Weighted accurately 2.38 gm disodium hydrogen phosphate, 0.19 gm potassium dihydrogen phosphate, and 8 gm sodium chloride and dissolved in 1000 mL of water.
Procedure:
The study was performed by modified Franz diffusion cell using Cellophane membrane. Before carrying out the study, membrane was kept in phosphate buffer pH 7.4 for 24 hr and it was mounted carefully between the donor and receptor chamber. 1 gm of gel was weighed and homogeneity spread on the dialysis membrane. 5 ml of acetate buffer (pH 7.4) was placed in receptor medium as dissolution media. Both donor and receptor compartment were kept in contact with each other and whole assembly was maintained at constant temperature of 32 ± 0.5°C. Magnetic bead was used to stirred the solution of receptor chamber. 5 ml of sample was withdrawn after specific time intervals and equal amount was replaced with fresh dissolution media. Sample absorbance was calculated spectrophotometrically at 272 nm and % cumulative drug permeation was calculated.

Fig No.3

RESULT & DISCUSSION

Parameters	Observation
Gel apperance	Clear
Homogenecity	Good
Extrudability	Good
pH	6.7
Spreadability	22.16
Grittiness	Absent
Viscosity	1986 cps
Drug Content	90.75 %

Table No.3

Batches	F1	F2	F3
pH	6.5	6.4	6.6
Spreadability	19.45	21.38	20.48
Appearance	Clear	Clear	Clear
Grittiness	Absent	Absent	Absent
Viscosity	1894 cps	1980 cps	1916 cps
Homogenecity	Good	Good	Good

Table No.4

Evaluation	Batch 1		Batch 3	
	Initial	After	Initial	After
pH	6.6	6.7	6.7	6.7
Appearance	Good	Good	Good	Good
Viscosity	1894cps	1890cps	1916cps	1910cps
Spreadability	19.45	19.50	20.48	20.56

Table No.5 Stability study

Dye test : Dye test was carried out by using the water soluble dye ie. Sudan red. The little quantity of dye was dissolved in small quantity of water and it was

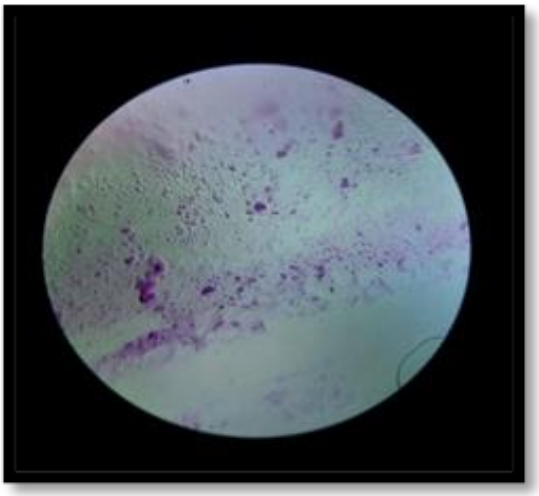

Fig No.4

pour on slide where gel was applied and wait to stain the formulation &staining was evaluated under microscope. If aqueous phase is stained it means it is o/w type of emulsion , while the oily phase is stained it means it is w/o type of emulsion.

Spreadability test:

Spreadability = m*l/t

=21.30 ×7.5/23.36

=6.8

Where, S=Spreadability (gcm/sec)

m = weight tied to the upper slide (20 grams)

l = length of glass slide (6cms).

T = time taken is seconds.

Appearance: The appearance of the gel formulation was observed by visual

Viscosity: viscosity of the gel formulation was done by using brook field viscometer at temperature 25C using spindle no 64 at 10 rpm.

In vitro drug release: In vitro drugrelease is determined by franz cell diffusion using cellophane membrane.

Time interval	F1	F2	F3
30 min	24	26	25
60 min	35	38	36
90 min	42	47	44
120min	51	50	52
150 min	63	68	65
180 min	78	80	77
210 min	87	85	84
240 min	92	89	88

Table.No.6

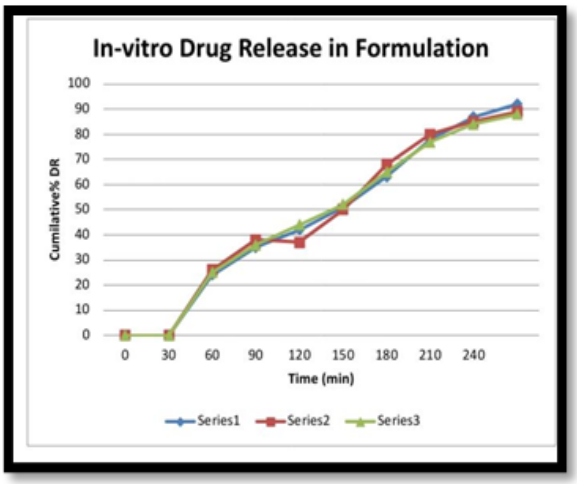

Fig.No.5

CONCLUSION

Topical gels containing Nyctantus Arbor Tritis extract can be successfully prepared Using carbopol-934 as gelling agents. The topical gel prepared from mixture carbopol-934 and batch 2 will be found to be better gelling agent for making an ideal topical preparation. extract in the form of gel possess significanttopical anti-inflammatory properties, supporting their traditional Use for the treatment.

REFERENCE

[1]. P. Bantawa, et. Al. Determination of essential oil contents and micro propagation of Gaultheria Fragrantissima, an endangered woody aromatic plant of India. The journal of horticultural science andBiotechnology 2011; 479-485.

[2]. V. Stankovet. Al. Definition of Inflammation Causes of Inflammation and Possible Anti-inflammatory Strategies. The open inflammation journal 2012; 5: 1-9.
[3]. G. Dixit, et. Al. Formulation and evaluation of polyherbal gel for anti – inflammatory activity. International Journal of pharmaceutical sciences and research 2013; 4 (3):1186- 1191.
[4]. A. Marcon, et.al. Carboxy fullerenes protect human keratinocytes from ultraviolet-B- induced apoptosis. J Invest Dermatol 2000; 115(5):835-41.
[5]. A. Huczko. Fullerenes: experimental evidence for a null risk of skin irritation and allergy. Fullerene SciTechnol 1999; 7:935-9.
[6]. S. Nayank , et. Al. "The Indian Pharmacist", Vol. III, No. 27, Sept. 2004, 7-14.
[7]. . Marcon, et.al. Carboxyfullerenes protect human keratinocytes from ultraviolet-B- induced apoptosis. J Invest Dermatol 2000; 115(5):835-41.
[8]. A. Huczko. Fullerenes: experimental evidence for a null risk of skin irritation and allergy. Fullerene SciTechnol 1999; 7:935-9.
[9]. S. Nayank , et. Al. "The Indian Pharmacist", Vol. III, No. 27, Sept. 2004, 7-14.
[10]. Matillha, "Antioxidants", Annu. Rev. Biochem., 1947, 177-192.
[11]. Jain N.K., et. Al., "Pharma Times", 2000, 21.Walfg, "The Discovery of the Antioxidant Function of Vitamin E", J. Nutr.2005; 135(3):358-366.
[12]. S. Walter, et. Al. Therapeutic transdermal drug innovation from 2000 to 2014: current status and outlook. Drug Discovery Today 2015; 20(11):1293-1299.
[13]. J. Hadgraft, et. Al. Skin: the ultimate interface, Physical Chemistry Chemical Physics.2012; 13(12): 5215 -5222.
[14]. W. Rui Liu, et.al. Review Gaultheria: Phytochemical and Pharmacological Characteristics. Molecule 2013; 12071-12108.
[15]. ALiu, W.-R.; Qiao, W.-L.; Liu, Z.-Z.; Wang, X.-H.; Jiang, R.; Li, S.-Y.; Shi, R.-B.; She, G.-M. Gaultheria: Phytochemical and Pharmacological Characteristics. Molecules 2013, 18, 12071-12108
[16] Dixit G., Misal G., gulkari V., Upadhye K. Formulation and evaluation of polyherbal gel For anti-inflammatory activity. IJPSR. 2013: 4(3): 1186-1191.
[17] Mishra U.S., Murthy P.N., Pasa G., Nayak R.K. Formulation and evaluation of herbal
[18] Chatterjee P., Chandra S., Dey P., Bhattacharya S. Evaluation of antiiflammatory effects Of green tea and black tea: A comparative in vitro study. J.Adv.Pharm.Tech.Res. 2014:3(2): 136-138
[19] Surekha B Brawl, Mohammed Shakir Ghouse, Amruta S Wattamwar, Ajit M Murkute (2017) A Comprehensive Review on Night-flowering Jasmine Nyctanthes arbor-tristis. Journal of Medical and Pharmaceutical Innovation 4(19): 1-6.
[20] Aggarwal SG, Goyal S (2013) Nyctanthusarbor-tristis against PathogenicBacteria. Journal of Pharmacognosy and phytochemistry 2(3): 124-127.
[21] Geetha DH, Rajeshwari M (2014) Anti-bacterial activity of Leaf of Nyctanthus Linn. International Research Journal of Nyctanthusarbortristis Linn. International Research Journal of Pharmaceutical and applied sciences 4(4): 4-6