Formulation and Evaluation of Semi-Synthetic Gel Containing Tagetes Erecta and Curcumin Extract for the Treatment of Atopic Dermatitis (Eczema)

Miss. Anuradha Sanjay Gatane[1], Asst. Prof. Miss. Sujata Umakant Veer[2], Asst. Prof. Miss. Neha Sunil Garud[3]

[1]Student, Final year B. Pharmacy, [2, 3]Assistant Professor
Saikrupa Institute of Pharmacy, Ghargaon, Shrigonda, Ahilyanagar, Maharashtra, India 413728

Corresponding Author:
Asst. Prof. Ms. Veer Sujata Umakant,
Assistant Professor, Saikrupa Institute of Pharmacy, Ghargaon, Shrigonda, Ahilyanagar, Maharashtra, India 413728
Email Id: sujataveer22@gmail.com
Mobile: 8380002675

Abstract

Atopic dermatitis is a chronic inflammatory skin condition characterized by dry, itchy and inflamed skin, significantly impacting the quality of life of affected individuals. Current treatments often involve topical corticosteroids, immunomodulators and moisturizers but these may have limitations such as side effects, limited efficacy.This study aimed to formulate and evaluate a semi- synthetic gel formulation integrating natural phytochemicals from *Tageteserecta*(commonlyknown as marigold) and *Curcumin*- to botanicals known for their anti-inflammatory, antioxidant and wound healing properties.

The objective of this study was to formulate, optimize and evaluate a semi-synthetic gel incorporating extracts from *Tagetes erecta* and *curcumin* for potential therapeutic application in the management of atopic dermatitis. The gel was formulated using a combination of natural and synthetic polymers, including carbapol and triethanolamine and evaluated for its physical, chemical and microbiological properties. The gel showed good spreadability, pH and viscosity and was found to be stable under various storge conditions. In vitro studies demonstrated the gel's anti-inflammatory and antioxidant properties and its ability to reduce inflammation and oxidative stress. The anti-inflammatory effects of gel were attributed to the presence of flavonoids and carotenoids in *Tageteserecta* and *Curcumin*, which inhibited the production of pro-inflammatory cytokines and enzymes. The antioxidant properties of a gel were also attributed to the presence of these bioactive compounds, which neutralized free radicals and reduced oxidative stress.

The results suggest that the semi-synthetic gel containing *Tagetes erecta* and *Curcumin* extracts may be a promising treatment option for atopic dermatitis, offering a natural and effective alternatives to conventional treatments. The gel's stability, spreadability and anti-inflammatory and anti-oxidant properties make it an attractive option for topical application.

Keywords: Atopic dermatitis, semi-synthetic gel, *Tagetes erecta*, *Curcumin*, anti-inflammatory, antioxidant, topical application

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin condition that affects millions of people worldwide.[1] It is characterized by dry, itchy and inflamed skin and can significantly impact the quality of life of affected individuals.[2] Atopic dermatitis can affect anyone, regardless of age and is often associated with other allergic conditions, such as asthma and rhinitis.[3] Current treatments for AD often involved topical corticosteroids, immunomodulators and moisturizers. [4] While these treatments can provide relief, they may have limitations, such as side effects, limited efficacy or inconvenience.[5] Long term used of topical corticosteroids, for example, can lead to skin thinning, telangiectasia and other adverse effects.[6]

In recent years, there has been a growing interest in natural remedies for AD, including herbal extracts and phytochemicals.[7] These natural compounds may offer a safer and more effective alternative to conventional treatments, with fewer side effects and improved patient outcomes.[8]*Tagetes erecta*and *Curcumin* are two natural compounds that have shown promise in reducing inflammation and oxidative stress.[9,10]*Tagetes erecta*also known as marigold, has been used in traditional medicine for its anti-inflammatory and anti-oxidant properties.[11]*Curcumin*, a polyphenol derived from turmeric, has potent anti-inflammatory and anti-oxidant effects and has been shown to inhibit the production of pro-inflammatory cytokines and enzymes.[12] The herb, Sunset-yellow Curcuma longa, also known as C. longa, is a spice with anti-inflammatory, antibacterial, and antioxidant qualities that is used in wound healing.[13] Its use prevents eczema and psoriasis, and decreases outbreaks that are already present. In the present study, we formulated a gel, which is a stiff jelly-like substance with texture ranging from soft and weak to rigid and durable.[14] Gels are highly diluted crosslinked systems that, in their steady state, do not flow. Gels possess liquid characteristics, but because of a three-dimensional cross-linked complex inside the liquid, they behave like solids.[15,16] Turmeric powder consists of 60-70% carbohydrates, 6-8% protein, 3-7% dietary minerals, 5-10% fat, 3-7% essential oils, 2-7% dietary fiber, and 1-6% curcuminoids. Phytochemical components of turmeric consist of diarylheptanoids, for example, curcumin, demethoxycurcumin, and bisdemethoxycurcumin. A number of essential oils are present in turmeric, among which turmerone, atlantone, zingiberene, and germacrone are major constituents. *C. longa* has been reported to possess anti-inflammatory, antioxidant, and anti-aging activities as well as the ability to reduce dandruff and itch.[17]

Tagetes erectaL. is an annual herb belonging to family Asteraceae which is known as marigold. In Thai-land, the flowers are primarily used for decoration in Buddhist festivals, weddings, and politics. The flower is plentiful of different classes of phytochemicals, such as carotenoids, phenolic acids, and flavonoids. These com- pounds were reported to be responsible for several pharmacological activities such as antioxidant, antimicrobial, hepatoprotective, analgesic, and wound healing activities. The antibacterial activities of flavonoids have been indicated by many researchers using different assays such as agar dilution technique, paper disk diffusion assay, hole- plate diffusion method, and broth microdilution technique. The flavonoids and their glycosides from marigold flower such as quercetagetin, quercetagitrin, patuletin, and pituitrin were reported to possess antibacterial activities against some Gram-positive and Gram-negative bacteria. Consequently, the marigold flower could be a possible source of antibacterial agents.[18] The present study aims to formulate topical gel of *T. erecta* floral extract for treatment of skin infections. The extract with the highest antibacterial activity was selected to formulate as topical gel. Physical properties and antibacterial activity of the gel were also investigated.

Atopic Dermatitis (Eczema)

Atopic dermatitis, also known as atopic eczema, is a chronic inflammatory skin condition characterized by pruritic, erythematous and scaly skin lesions often localized to the flexural surfaces of the body (*Figure 1*). It can present with asthma and allergic rhinitis as part of an allergic triad; an estimated 30 percent of children with atopic dermatitis develop asthma later in life.[19] The onset of atopic dermatitis generally is before two years of age, with only 10 percent of cases diagnosed after five years of age.[20] A 2003 survey of children in the United States estimated an overall prevalence of approximately 11 percent, and as high as 19 percent in some states.[21] A 2007 U.S. population-based survey suggested an estimated 17.8 million persons are living with atopic dermatitis, and most cases have not been diagnosed.[22] Early diagnosis and treatment may prevent significant morbidity from sleep disturbances, chronic post inflammatory skin changes, scarring from picking and scratching, and the development of secondary skin infections with Staphylococcus, Streptococcus, and herpes species.[23]

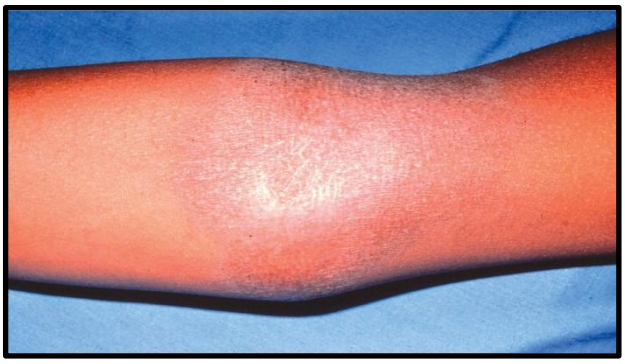

Figure 1: Atopicdermatitis on flexural surface of the arm

A genetic defect in the filaggrin protein is thought to cause atopic dermatitis by disrupting the epidermis. This disruption, in turn, results in contact between immune cells in the dermis and antigens from the external environment leading to intense itching, scratching, and inflammation.[24]Scratching can then lead to further disruption and inflammation of the epidermal skin barrier; this has been described as the itch scratch cycle. Atopic dermatitis can present in three clinical phases. Acute atopic dermatitis presents with a vesicular, weeping, crusting eruption (*Figure 2*). Subacute atopic dermatitis presents with dry, scaly, erythematous papules and plaques (*Figure 3*). Chronic atopic dermatitis demonstrates lichenification from repeated scratching (*Figures 4 and 5*). A more subtle presentation of atopic dermatitis that commonly occurs in children is pityriasis alba, which is characterized by hypopigmented, poorly demarcated plaques with fine scale. Atopic dermatitis tends to involve the flexural surfaces of the body, anterior and lateral neck, eyelids, forehead, face, wrists, dorsa of the feet, and hands. Because atopic dermatitis has many appearances, the differential diagnosis is broad.[25]

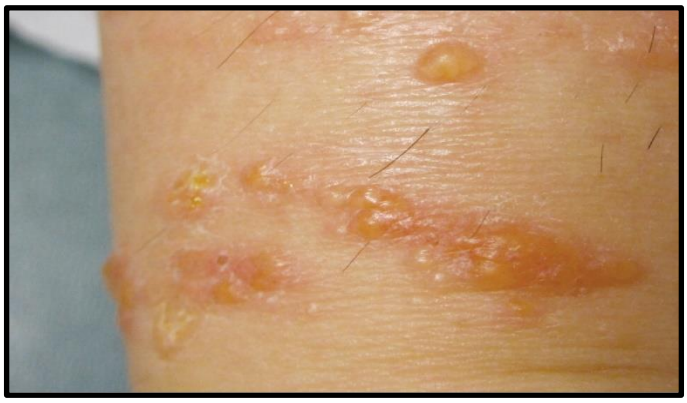

figure 2: Acute AD in its weeping, blistering form

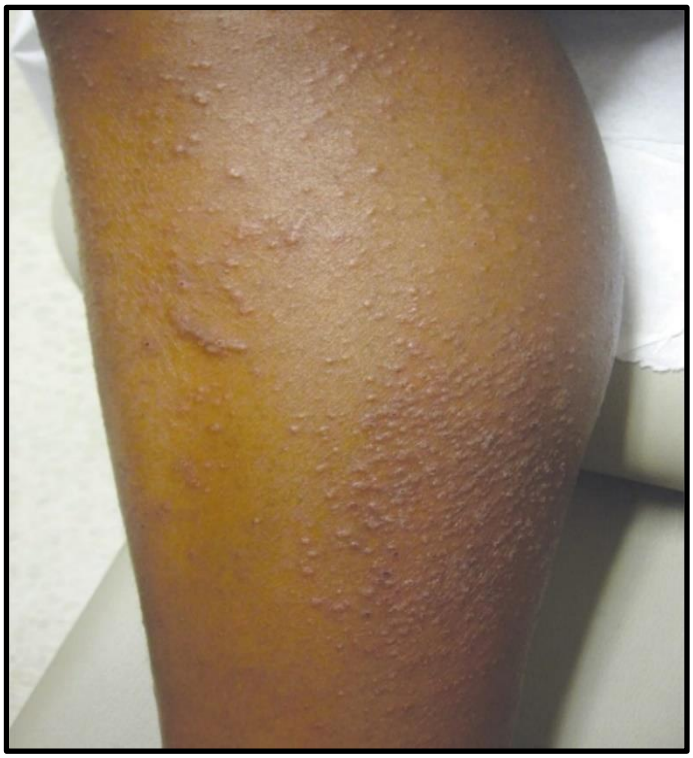

figure 3: Subacute Adin its dry, scaly, papular form

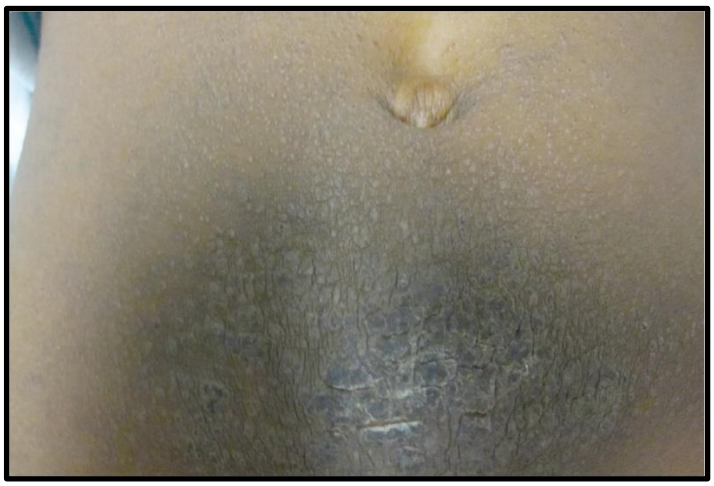

figure 4: Chronic AD in its lichenified form

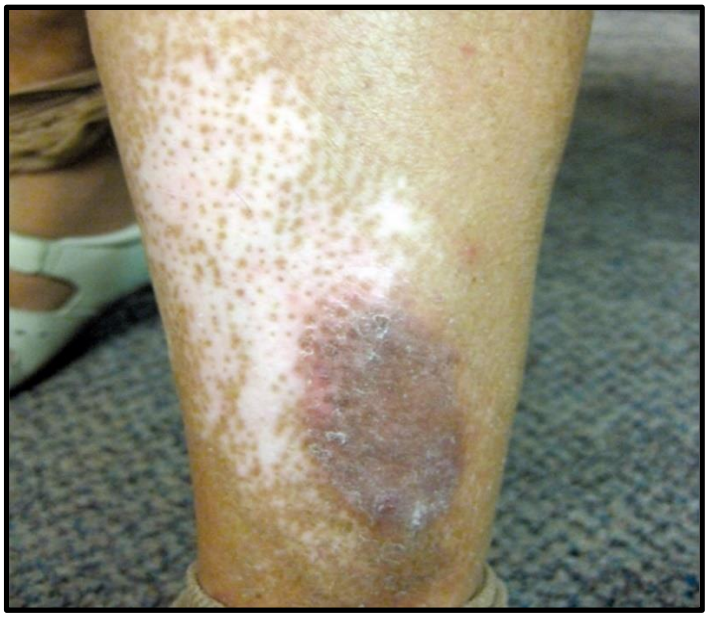

figure 5: Chronic AD demonstrating a lichenified plague as well as depigmentation

Patients with atopic dermatitis are also at risk of developing herpes simplex virus infection, known as Kaposi varicelliform eruption or eczema herpeticum. Eczematous skin enables a localized herpes outbreak to spread over the skin and create a painful papulovesicular rash (*Figure 6*). Other complications of atopic dermatitis include scars from picking and scratching, chronic post inflammatory skin changes, and skin atrophy from long-term treatment with topical corticosteroids.

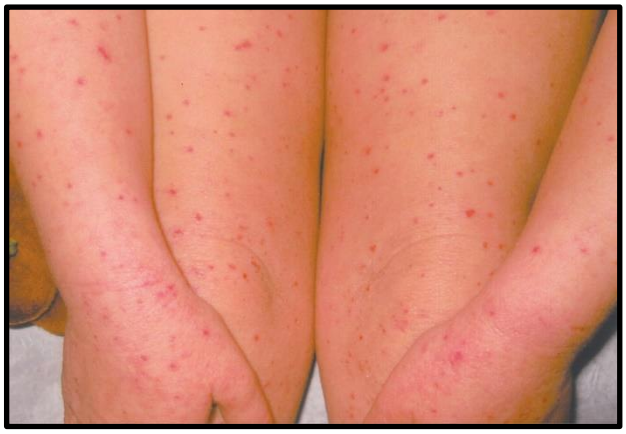

figure 6: Ezema herpeticum in a young girl

Xerosis (skin dryness) is a common finding in atopic dermatitis, and many patients attest that control of their xerosis mirrors control of their dermatitis (*Figures 7 and 8*).

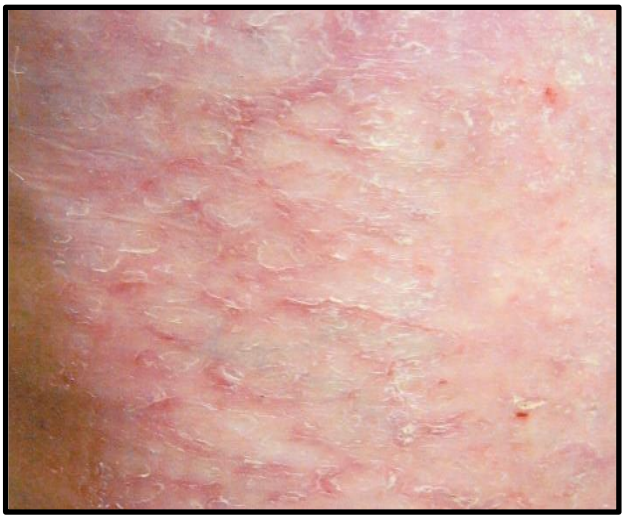

figure 7: Close up photograph of the skin demonstrating dramatic xerosis

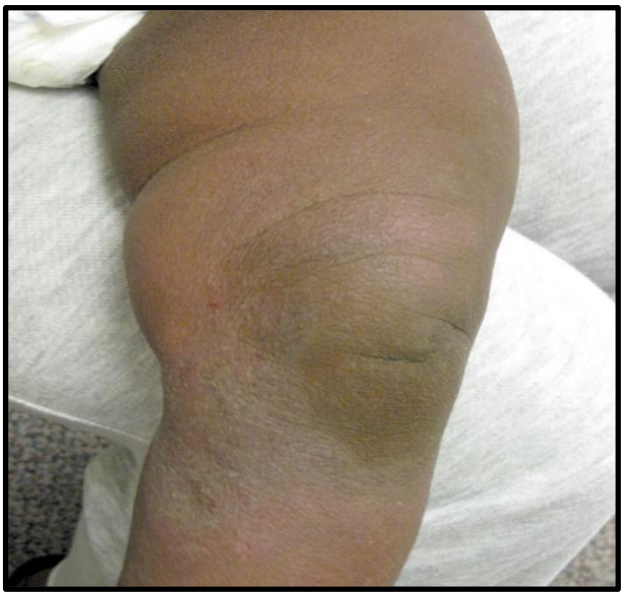

figure 8: Leg of an infant with AD demonstrating xerosis

The principal complication of prolonged application of topical corticosteroids, especially those of higher-potency, is skin atrophy (Figure 9). Other local complications include telangiectasia, striae, hypopigmentation, and corticosteroid acne. Although high-potency agents have some potential for systemic absorption that leads to problems of adrenal suppression and growth retardation in children, this is uncommon and has not been observed with continuous use of mild- or moderate-potency corticosteroids.[26,27]

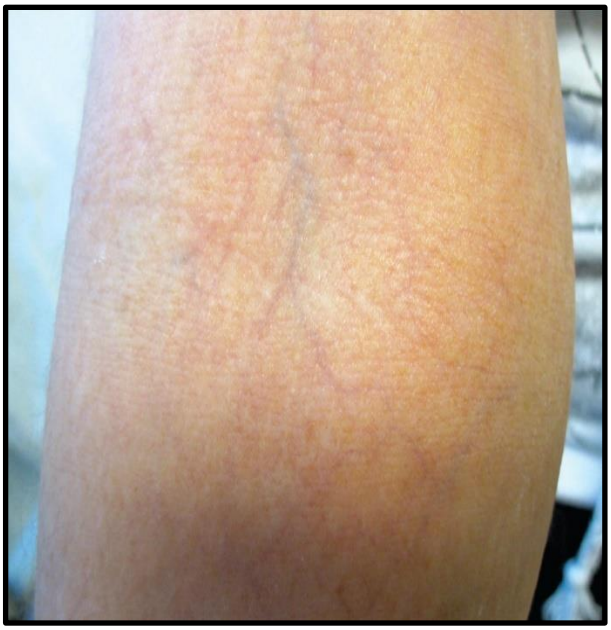

figure 9: Atrophy on flexural surface of arm caused by long term application of topical corticosteroid

Symptoms of AD

Atopic dermatitis (eczema) symptoms can appear anywhere on the body and vary widely from person to person. They may include

1. Dry, scaly skin- This skin tends to loose moisture easily, leading to dryness and flakiness.
2. Itching- Often intense and persistent, especially at night; considered a hallmark symptoms of AD.
3. Red to brownish-gray patches- Typically appear on the hands, feet, ankles, wrists, neck, upper chest, eyelids, and in the bend of the elbows and knees.
4. Thickened, cracked skin- A result of chronic scratching and rubbing.
5. Swelling and inflammation- Skin may appear swollen and sensitive to touch.
6. Skin infections- Due to scratching, the affected skin can become open to bacterial or viral infections, often appearing as oozing or crusted sores.[28]

PLANT PROFILE

1. **Curcuma longa**

Figure 10: Curcuma longa

Turmeric is a rhizome of ginger like plant. The plant is an herbaceous perineal, 60-90cm high with a short stem tufted leaf. Its flowers are yellow, between 10-15cm in length and they group together. No fruits are known for this plant. The rhizome is yellowish-brown with a dull orange interior that looks bright yellow when powdered. Rhizome measures 2.5-7.0cm in length and 2.5cm in diameter. It was prescribed for the treatment of many medical problems ranging from constipation to skin disease.

Synonym- Indian saffron, turmeric, haldi, Curcuma longa

Biological source- *Curcumin* is primarily source from the dried as well as fresh rhizomes of the curcuma longa plant.

Chemical constituents- Major constituents of *curcumin* is 50-60% of essential oil 2-7% with high content bisabolane derivates. It also contain Desmethoxycurcumin (DMC), Bisdesmethoxycurcumin (BDMC), common phytosterols , ar-tumerone, zingiberene fatty acids and polysaccharides.

Scientific classification

Kingdom:Plantae

Order: Zingiberales

Family:Zingiberaceae

Genus:Curcuma

Species:Longa

Uses- It suppresses symptoms associated with arthritis.

- It lower serum cholesterol levels.
- It enhances wound healing.
- It stimulates muscle regeneration.

2. Tagetes erecta

Figure 11: Tagetes erecta

Tagetes erecta is a herbaceous annual or perennial plant whose height ranges from 30-110 cm. The root is cylindrical, pivotig with a fibrous and shallow branching system. The stem is striated, sometimes ridged.

Members of the genus tagetes have attractive yellow, orange or red composite flowers that are solitary on the stems or clustered.

Synonyms- African marigold, Aztec marigold, and Big marigold, Mexican mariglod.

Biological Source- The biological source for *Tagetes erecta* is the plant itself.

Chemical constituents- It contain variety of chemical constituents including carotenoids, flavonoids, and esssential oil. Specifically plant contain carotenoids like lutein and zeaxanthin as well as flavonoids like quercetin.

Scientific classification

Kingdom: Plantae

Order: Asterales

Family: Astereceae

Genus: Tagetes

Species: Erecta

Uses- It has variety of uses, including traditional applications (to treat various ailments, including fevers, liver complaints, scabies and eye problem), in food and beverage flavoring. It is also used as a natural dye and for its pest repelling properties in garden. It also act as anti-inflammatory, antimicrobial, antipyretic, antiepileptic and antioxidant.

MATERIAL AND METHODS

Material

1 Chemical-

Sr.no.	**Chemicals**
1.	*Curcumin* extract
2.	*Tagetes erecta* Extract
3.	Carbapol 940(gm)
4.	Methanol
5.	Triethanolamine(ml)
6.	Methyl paraben
7	Propyl paraben
8	Purified water

2. Glassware-

Sr.no.	Glassware
1.	Beaker
2.	Measuring cylinder
3.	Glass rod
4.	Funnel
5.	Pipette

3 Instrument

Sr.no	Instrument
1.	Digital weighing balance
2.	PH meter

METHOD:-

The extraction of crude drug was carried out for *Tagetes erecta* leaves and the *curcumin* powdered was purchased from local market.

Extraction procedure for *tagetes erecta* leaves:-

1. Maceration of *Tagetes erecta* leaves in Methanol

-leaves are washed with distilled water and dried for 48 hrs until it dry totally.

-dried leaves were subjected for the grinding by small grinder

-Take 50 g of dried grinding powder and soak it in 250 ml of methanol for 24 hrs.

-After soaking filter the extract by using whatman no.1 filter paper

-Collect the filtrate and evaporate all solvent present in the filtrate

-Lastly collect the dried extract and stored.

Figure 12: Extraction of tagetes erecta leaves

Procedure for formulation of a gel:-

- Weigh *tagetes erecta* and *curcumin* extracts accurately and mix them in the specific amount of purified water.

- Weigh carbapol accurately and disperse carbapol in purified water and then mix well to create uniform gel base.

- Add API mixture to the gel base and mix well. Ensures uniform distribution of the APIs mixture in the gel base.

- Weigh methyl paraben and propyl paraben accurately and add them to the gel and mix well.

- Use triethanolamine to adjust the pH of the gel to suitable range (5.5-6.5)

- Mix the gel well to ensure uniform distribution of ingredients. Check the gels physical appearance, pH and viscosity.

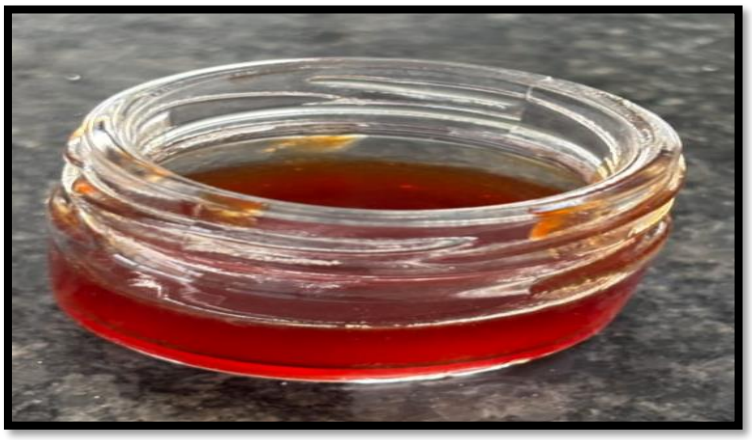

Figure 13: Formulated gel

Formulation table:-

Sr.	Material	F 1	F 2	F 3	F 4	F 5	Roles

no							
1.	*Curcumin* extract	0.3	0.3	0.4	0.5	0.6	Active ingredient
2.	*Tagetes erecta* extract	0.3	0.3	0.4	0.5	0.6	Active ingredient
3.	Carbapol	1.0	0.5	0.5	0.5	0.5	Gelling agent
4.	Methyl paraben	0.2	0.2	0.2	0.2	0.2	Preservative
5.	Propyl paraben	0.5	0.6	0.7	0.7	0.7	Stabilizer
6.	Triethanolamine	1	1	1	1	1	Improves texture and facilitates easy spreadability
7.	Distilled water	q.s	q.s	q.s	q.s	q.s	Solvent

Evaluation parameter: -

1. Physical appearance

Physical parameter such as color and appearance were checked visually and reported in table no 1.

2. Stability

The stability studies was conducted for 4 weeks and the results was reported in table no 2.

3 PH

pH of the gel was measured by using digital pH meter. 1gm of gel was taken and dispersed in 10 ml of distilled water and keep away for two hours. The dimension of pH of expression was carried out in three times and the average values are reported. pH of gel expression was reported in table 3.

4 Spreadability

The spreadability was measured by placing 0.5 g of gel within a premarked circle of diameter 1 cm on a glass plate over which a second glass plate was placed and 50 g weight was allowed to rest on the upper glass plate for a period of 5 min. Spreading of the gel caused an increase in diameter of the circle, which was measured in cm and noted down. These results were taken as comparative values for spreadability. Results was reported in table no 4.

$$S = M * L / T$$

WhereM =Weight in the pan which is tied to the upper slide

L=length moved by the glass slide

T=time in second taken to separate the slide completely each other.

Standard value:- 17.21-25.48 gm.cm\sec

5 Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels had set in the container. They were checked for their appearance and presence of any aggregates. Results was reported in table no 5.

6 Clarity

Visual assessment was conducted to ascertain the clarity of each batch an was reported in table no 6.

RESULT AND DISCUSSION:-

Test	Appearance
PH	5.56
Stability	Stable
Color	Brownish
Spreadability	19.91
Homogenicity	Very good
Clarity	Clear

Discussion:-

The appearance of the formulation was good and variation in the pH occurs. The initial stability batch stability was remained same. No Color change occurs in the stability period.

1.Physical appearance-

Observation: Table no 1

Gel formula	Appearance
Formulation 1	Dark brown
Formulation 2	Marron
Formulation 3	brownish
Formulation 4	Light brownish
Formulation 5	Brownish

2.Stability:

Observation: Table no 2

Gel formula	1st week	2nd week	3rd week	4th week
Formulation 1	Stable	Stable	Instable	Stable
Formulation 2	Stable	Stable	Instable	Instable
Formulation 3	Stable	Stable	Instable	Instable
Formulation 4	Stable	Stable	Stable	Stable
Formulation 5	Stable	Stable	Stable	Stable

3.Measurement of pH

Observation: Table no 3

Gel formula	PH
Formulation 1	7.00
Formulation 2	6.49
Formulation 3	6.72
Formulation 4	6.75
Formulation 5	5.56

4.Spreadability

Observation: Table no 4

Gel formula	Spreadability
Formulation 1	17.3
Formulation 2	15.3
Formulation 3	25.6
Formulation 4	22.91
Formulation 5	19.91

5. Homogeneity

Observation: Table no 5

Gel formula	Homogeneity
Formulation 1	Good
Formulation 2	Good
Formulation 3	Moderate
Formulation 4	Moderate
Formulation 5	Very good

6.Clarity

Observation: Table no 6

Gel formula	.Clarity
Formulation 1	Clear
Formulation 2	Clear
Formulation 3	Very clear
Formulation 4	Clear
Formulation 5	Clear

CONCLUSION

From the present research work it was concluded that, the gel prepared by combination of Turmeric and *Tagetes erecta* leaves extract for the treatment of Atopic dermatitis was successful extracted by maceration. *Tagetes erecta* and *curcumin* were chosen as APIs due to their individual and potential synergistic benefits in reducing inflammation and oxidative stress, which is key factors in atopic dermatitis. Their combination may provide a comprehensive approach to treating the condition and their natural origin and relatively safe profile make them an attractive option for future research and development.

These two extracts were also tested for the identification of compounds present in it and it was found that, *curcumin* was present in turmeric whereas quercetin was present in the *Tagetes erecta* leaves extract in the more concentration

The formulated gel was analyzed for the different properties and also Antibacterial activities against various strains of microbes. The prepared gel of turmeric with *Tagetes erecta* leaves extract will be the breakthrough for the neutraceutical industries if it is studied in more prospective way.

REFERENCES

1. Leung DY, et al. (2003). Atopic dermatitis. Lancet, 361(9363), 151-160.

2. Bieber T. (2008). Atopic dermatitis. N Engl J Med, 358(14), 1483-1494.

3. Spergel JM, et al. (2003). Atopic dermatitis and the atopic march. J Allergy Clin Immunol, 112(6), S118-S127.

4. Hanifin JM, et al. (2010). Guidelines of care for the management of atopic dermatitis. J Am Acad Dermatol, 62(2), 295-306.

5. Hoare C, et al. (2000). New treatments for atopic dermatitis. Clin Exp Dermatol, 25(7), 559-565.

6. Hengge UR, et al. (2006). Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol, 54(1), 1-15.

7. Zhang Y, et al. (2018). Natural products for the treatment of atopic dermatitis. J Clin Med, 7(10), 271.

8. Gupta SC, et al. (2013). Therapeutic roles of curcumin: Lessons learned from clinical trials. AAPS J, 15(1), 195-218.

9. Kasiram MI, et al. (2017). Tagetes erecta: A review of its phytochemical and pharmacological properties. J Ethnopharmacol, 198, 128-144.

10. Kumar A, et al. (2018). Curcumin: A natural anti-inflammatory agent. J Biol Chem, 293(15), 5625-5634.

11. Srivastava JK, et al. (2010). Chamomile: A herbal medicine of the past with a bright future. Mol Med Report, 3(6), 895-901.

12. Kunnumakkara AB, et al. (2018). Curcumin inhibits proliferation, migration, and invasion of cancer cells. Adv Exp Med Biol, 1037, 127-147.

13. Tapsell LC et al. Health benefits of herbs and spices: the past, the present, the future. Med J Aust. 2006 Aug 21; 185(4 Suppl): S4-24.

14. Huffman MA. Animal self-medication and ethno-medicine: exploration and exploitation of the medicinal properties of plants. Proc Nutr Soc 2003; 62 (2): 371-81.

15. Girish Dwivedi, Shridhar Dwivedi. History of Medicine: Sushruta the Clinician - Teacher par Excellence. National Informatics Centre 2007; 224-225.

16. Ernst E. Herbal medicines: balancing benefits and risks. Novartis Found. Symp.2007; 282: 154-67; discussion 167-72, 212-8.

17. Paul A.J. Kolarsick, BS, Maria Ann Kolarsick, Anatomy and Physiology of the Skin. Andrews' Diseases of the Skin: Clinical Dermatology (10th ed., p. 1)

18. Riviere JE, Structure and Function of Skin. In book: Dermal Absorption Models in Toxicology and Pharmacology (pp.1-19)

19. Spergel JM. Epidemiology of atopic dermatitis and atopic march in children. Immunol Allergy Clin North Am. 2010;30(3):269-280.

20. Wolff KL, Johnson RI. Atopic dermatitis. In: Wolff K, Johnson RA, Fitzpatrick TB. Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology. 6th ed. New York, NY: McGraw-Hill Medical; 2009:34–36.

21. Shaw TE, Currie GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. J Invest Dermatol. 2011;131(1):67-73.

22. Hanifin JM, Reed ML Eczema Prevalence and Impact Working Group. A population-based survey of eczema prevalence in the United States. Dermatitis. 2007;18(2):82-91.

23. Lewis-Jones S. Quality of life and childhood atopic dermatitis: the misery of living with childhood eczema. Int J Clin Pract. 2006;60(8):984-992.

24. Maintz L, Novak N. Getting more and more complex: the pathophysiology of atopic eczema. Eur J Dermatol. 2007;17(4):267-283.

25. Leung DY, Bieber T. Atopic dermatitis. Lancet. 2003;361(9352):151-160.

26. Levin C, Maibach HI. Topical corticosteroid-induced adrenocortical insufficiency: clinical implications. Am J Clin Dermatol. 2002;3(3):141-147.

27. Ellison JA, Patel L, Ray DW, David TJ, Clayton PE. Hypothalamicpituitary-adrenal function and glucocorticoid sensitivity in atopic dermatitis. Pediatrics. 2000;105(4 pt 1):794-799.

28.Silverberg, J. I. (2017). Atopic dermatitis: Epidemiology and risk factors. In Journal of Allergy and Clinical Immunology, 140(2), 349–356