



DEVELOPMENT AND EVALUATION OF HERBAL CREAM FOR RHEUMATISM

Ranganathan K^{*1}, Jeevanandham S², Nandhini.A³, Preethi.M⁴, Rinshida P.A⁵, Sakthivel.M⁶, Mohammed Basith.M⁷

^{1*, 2, 3, 4, 5, 6, 7}Department of Pharmaceutics, Sree Abirami college of Pharmacy, Eachanari, Coimbatore – 641 021, India

***Corresponding Author:-** Ranganathan K

*Department of Pharmaceutics, Sree Abirami college of Pharmacy, Eachanari, Coimbatore – 641 021, India

Abstract

Aim: The present study was to formulate and evaluate the herbal cream comprising extracts of different medicinal plants.

Experimental: Using a Soxhlet apparatus, an aqueous extract of all the chosen plants (*Morinda Tinctoria*, *Tridax Procumbens*) was created through a series of solvent extraction steps. A topical herbal cream was created and tested for several qualities, including stability, spreadability, pH, consistency, color, and viscosity. Using incision and excision wound models, a pharmacological assessment of a herbal cream formulation was conducted.

Result and Conclusion: It can be inferred from the results of the various evaluation parameters that the prepared herbal formulation was secure and safe to use in the process of wound healing.

Keywords: *Morinda Tinctoria*, *Tridax Procumbens*, Herbal Cosmetics, Anti-Inflammatory Cream

INTRODUCTION

Any illness characterized by pain and inflammation in the muscles, joints, or fibrous tissue is referred to as rheumatism; this includes rheumatoid arthritis. Arthritis refers to inflammation of the joints. One of your body's natural responses to illness or injury is inflammation. It consists of stiffness, pain, and swelling. Tissue damage can result from persistent inflammation or from inflammation that recurs, as in the case of arthritis. It is an ongoing inflammatory condition. One of the more prevalent autoimmune diseases, rheumatoid arthritis affects about 1% of the global population^[1]. It is characterized by inflammatory processes in the synovium of the joint, which destroy components of the bone and cartilage at joints and cause pain and incapacity. Although it may not have arrived in Europe until the 17th century, it was present in the early Native American population several thousand years ago. Autoantibodies and immune complexes were central to early theories regarding the pathophysiology of rheumatoid arthritis. The rheumatoid synovium's aggressive tumor-like behavior, T-cell-independent cytokine networks, and antigen-specific response have all been linked^[2]. The role of autoantibodies has come back into focus more recently. Certain therapeutic interventions are destroyed in rheumatoid arthritis based on the pathogenic mechanisms.

Most of the time, arthritis is not regarded as a serious public health issue. It rarely ends in death. For most forms, there is no known way to prevent them. On the other hand, among the most prevalent chronic conditions is arthritis. It is the main reason why elderly people become disabled and why they

are admitted to skilled nursing facilities^[3]. The effects of this disease on society—including decreased productivity and higher health care costs—will worsen as our population ages. It is estimated that the annual costs associated with arthritis, both direct and indirect, exceed \$31 billion.

The word "arthritis" describes over 100 conditions that affect the joints and/or the surrounding tissues, including the muscles, tendons, and bones. These illnesses are the leading cause of disability among the elderly and impact over 36 million Americans. Systemic lupus erythematosus and rheumatoid arthritis may also be linked to premature mortality, despite the fact that these conditions typically cause more morbidity than death. With rare exceptions, neither pharmacological nor behavioral therapies can prevent or treat these illnesses^[4]. The majority of types of arthritis require long-term care, just like other chronic diseases. Minimizing pain, disability, deformity, and the social/psychological dysfunction that frequently accompanies chronic, excruciating illnesses is the aim of management^[5]. Even though the number of medical and surgical procedures has increased, only a small percentage of arthritis sufferers benefit greatly from them.

PATHOLOGY OF RHEUMATOID ARTHRITIS:

It is an ongoing inflammatory condition. One of the more prevalent autoimmune diseases, rheumatoid arthritis (RA), affects about 1% of the global population^[6]. It is characterized by joint synovium inflammation, which destroys components of the bone and cartilage at joints, causing pain and incapacity.

Rheumatoid arthritis is caused by the interaction of an individual's genetic makeup with environmental factors (such as tobacco smoke and pathogens), which results in the alteration of our own antigens^[7]. For instance, IgG antibodies or other proteins such as vimentin or type 2 collagen. Citrullination is the process that causes this modification.



Fig No 1: Rheumatoid arthritis

HERBAL CREAM

Cream is defined as semisolid emulsions of the water in oil (w/o) or oil in water (o/w) type that are meant to be applied externally. Cream is divided into two categories: water in oil emulsion and oil in water. Its primary function is to stay longer at the application site when applied to the outer or superficial layers of the skin. A skin cream's purpose is to protect the skin from various environmental factors and weather conditions while also providing calming effects^[8]. Creams are water and oil emulsions that are semi-solid. They are separated into two categories: water-in-oil (W/O) creams, which are made of small water droplets scattered in a continuous oily phase, and oil-in-water (O/W) creams, which are made of small oil droplets dispersed in a continuous phase. Because oil-in-water creams are less greasy and easier to remove with water, they are more comfortable and acceptable from a cosmetic standpoint. Although creams containing water are more challenging to work with, many of the drugs that are added to them are hydrophobic and will come out of them more easily than from creams containing oil in water^[9]. Because they create an oily barrier that stops water loss from the stratum corneum, the skin's outermost layer, water-in-oil creams are also more moisturizing.

MATERIALS AND METHODS

INGREDIENTS	ROLES
<i>MORINDA TINCTORIA</i>	REDUCE INFLAMMATION
<i>TRIDAX PROCUMBENS</i>	REDUCE PAIN & INFLAMMATION
BORAX	EMULSIFYING AGENT
BEES WAX	GIVES THICKNESS TO CREAM, STABILIZER
LIQUID PARAFFIN	LUBRICATING AGENT
METHYL PARABEN	PRESERVATIVE

Table. No 1 Materials And Their Roles**Collection of plant materials**

The leaves of *Morinda Tinctoria* and *Tridax Procumbens* were gathered from a Coimbatore botanical garden.

Morinda Tinctoria**Fig.No 2:** Leaves Of *M. Tinctoria*

Synonyms : Nuna, Manjanathi, Indian mulberry

Family: Rubiaceae

Main constituent : Alkaloids, Triterpenoids, Tannins

Therapeutic uses : Anti-inflammatory, used in the treatment of RA externally.

Tridax Procumbens**Fig.No.3 :** Leaves Of *Tridax Procumbens*

Synonyms: Coat-buttons, Tridax daisy, Vettukkaaya-thazhai

Family: Asteraceae

Main constituent : Alkaloids, Steroids, Tannins

Therapeutic uses : Analgesic, Anti-inflammatory

EXTRACTION PROCESS***Morinda tinctoria* Extract Process**

Fresh, mature, and healthy *Morinda Tinctoria* leaves were gathered and cleaned with deionized water. then after it has fully dried. Ethanol was used to extract the dried leaves. To prepare the extracts, 10g of powdered leaf samples and 100ml of solvent were combined separately^[10]. The extracts were incubated for 48 hours at room temperature in a mechanical shaker. Following the incubation period, the contents were filtered using a funnel and filter paper. Additionally, the filter solution was dried, concentrated by letting the solvents evaporate, and refrigerated at 4°C until needed^[11].

***Tridax procumbens* Extract Process**

Fresh, healthy *Tridax procumbens* leaves were gathered, then cleaned in distilled water. then after it has fully dried. Ethanol was used to extract the dried leaves. To prepare the extracts, 10g of powdered leaf samples and 100ml of solvent were combined separately^[12]. The extracts were left to incubate at room temperature for 48 hours. Following the incubation period, the contents were filtered using a funnel and filter paper. After the solvents were evaporated, the filter solution was concentrated, dried, and refrigerated until needed again.

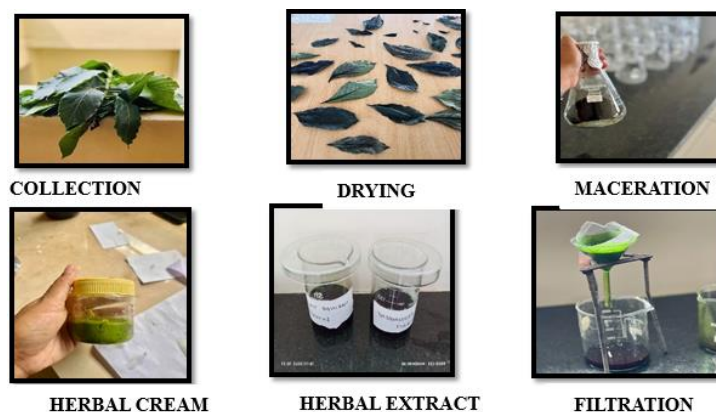


Fig.No 4: Extraction Process Of Plant Material

PHYTOCHEMICAL INVESTIGATION OF *MORINDA TINCTORIA*

PHYTOCHEMICALS	AEM
Saponins	+
Betacyanins	-
Alkaloids	+
Steroids	+
Terpenoids	+
Phenols	+
Glycosides	+
Volatile oils	+
Tannins	+

Table no:2 Phytochemical investigation of *M. Tinctoria*. (+) presence and (-) Absence

Utilizing water as a solvent, *Morinda Tinctoria* leaf extracts were made. The important phytochemicals found in *Morinda Tinctoria* (AEM) leaves that were extracted with water were qualitatively analysed^[13]. The findings showed that while betacyanin, alkaloids, and volatile oils are present, the AEM contains quinones, steroids, terpenoids, phenols, glycosides, and tannins.



FIG.NO 5: Phytochemical Analysis Of *Morinda Tinctoria*

Phytochemical investigation of *Tridax Procumbens*

Water was utilized as the solvent in the preparation of the leaf extracts from *Tridax Procumbens*. The major phytochemicals found in aqueously extracted *Tridax Procumbens* (AEM) leaves were subjected to a qualitative analysis^[14]. The findings showed that while betacyanin, alkaloids, and volatile oils are present, the AEM contains quinones, steroids, terpenoids, phenols, glycosides, and tannins.



Fig.No 6: Phytochemical analysis of *Tridax Procumens*

PHYTOCHEMICALS	AEM
Quinones	+
Betacyanins	-
Alkaloids	-
Steroids	+
Terpenoids	+
Phenols	+
Glycosides	+
Volatile oils	-
Tannins	+

Table no:3 Phytochemical investigation of *T. Procumbens* (+) presence and (-) Absence

FORMULATION OF CREAM

In a borosilicate glass beaker, heat liquid paraffin and beeswax to 75 °C and keep it there. Phase of oil. Borax and methylparaben should be dissolved in distilled water in a different beaker, and the mixture should be heated to 75 °C to produce a clear solution^[15]. (Phase of water). Add this aqueous phase to the heated oily phase gradually after that. Next, add a measured amount of *Tridax Procumbens* and *Morinda Tinctoria* extract, and mix well until a smooth cream forms^[16]. Place this cream onto the slab, stir it in a geometric pattern to combine all the ingredients and give it a smooth texture, and add a few drops of distilled water if needed. This process of preparing cream is known as the slab technique or the extemporaneous method^[17].

FORMULATION

INGREDIENT	F1	F2	F3	F4	F5
MORINDA TINCTORIA EXTRACT	3ml	3ml	3ml	3ml	3ml
TRIDAX PROCUMBENS EXTRACT	3ml	3ml	3ml	3ml	3ml
BORAX	0.2g	0.3g	0.4g	0.5g	0.6g
BEEES WAX	2g	2.5g	3g	3.5g	4g
LIQUID PARAFFIN	10ml	10ml	10ml	10ml	10ml
METHYL PARABEN	0.02g	0.02g	0.02g	0.02g	0.02g
DISTILLED WATER	q. s	q. s	q. s	q. s	q. s

Table. No 4 formulation



Fig No 7: Herbal cream formulation

EVALUATION OF CREAM

Physical evaluation

This test involved observing the cream's color, texture, state, and smell (table 3)^[18].

Irritancy

On the dorsal surface of the left hand, mark the area (1 cm²). After that, the area was treated with the cream, and the time was recorded^[19]. Next, for a period of up to 24 hours, it is examined for irritation, erythema, and oedema, if any, and reported (table 4).

Washability

The hand was treated with a small amount of cream and then rinsed with tap water (table 5).

pH

A digital pH meter was used to measure the pH after 0.5 g of cream had been distributed in 50 ml of distilled water (table 6)^[20].

Viscosity

Cream's viscosity was measured using a Brooke field viscometer at 25 °C and spindle number 63 spinning at 2.5 rpm (table 7)^[21].

Phase separation

The prepared cream was stored away from light and at a temperature between 25 and 100 °C in a closed container^[22]. Phase separation was then observed for 24 hours over a 30-day period. Any modifications to the phase separation were noted and verified (table 8)^[23].

Spreadability

The spreadability was measured by measuring the number of seconds it took for two slides separated by a cream layer under a specific load to separate from the cream. The better the spreadability, the shorter the time it takes to separate the two slides^[24]. Standard-sized glass slides were taken in two sets. After that, a slide with the right dimensions was chosen, and the cream formulation was put on it. After that, another slide was positioned above the formulation. The cream between the two slides was then uniformly compressed to form a thin layer by applying a weight or other load to the upper slide^[25]. After that, the weight was taken off, and any extra formulation that had stuck to the slides was scraped off. The force of the weight attached to the upper slide allowed it to slide off freely. It was noted how long it took for the upper slide to slip off (Table 9)^[26].

$$\text{Ability to spread} = m \times l/t$$

Where m is the standard weight (30g) that is fastened to or positioned over the upper slide.
l is the glass slide's length (5 cm)

t is the amount of time in seconds.

Greasiness

Here, the cream was smeared onto the skin's surface, and its oiliness or grease-like consistency was assessed (table 10)^[27].

Compatibility study

Using infrared spectroscopy, the herbal APIs' compatibility was investigated, and measurements of their solid state IR spectra were made. The measurement range for the infrared spectrum is 4000.12 to 525.03. There was a 75 sensitivity^[28]. The infrared spectra of the mixture of herbal APIs show the following characteristic peaks: 1026.79, 1368.24, 1438.73, 1604.78, 1728.45, and 3289.05 cm⁻¹. The infrared spectra of individual herbal APIs showed the same peaks as well (table 11, 12,13) (fig. 4, 5, 6)^[29].

RESULTS AND DISCUSSION

The evaluation outcomes for each of the five formulations are listed below.

Physical evaluation

The three formulations' states, textures, colors, and smells were examined in this test.

S.NO	PARAMETER	F1	F2	F3	F4	F5
1	Colour	Faint green	Faint green	Faint green	Faint green	Faint green
2	Odour	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant
3	Texture	Smooth	Smooth	Smooth	Smooth	Smooth
4	State	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid

Table No. 5 colour, odour, texture & state of the three formulations was checked

Irritancy

On the dorsal surface of the left hand, mark the area (1 cm²). After that, the area was treated with the cream, and the time was recorded. After that, it is observed for up to 24 hours and reported if there is any oedema, erythema, or irritation^[30]. The findings indicated that while F2H and F5H displayed mild irritation, all five formulations—F1H, F3H, and F4H—showed no signs of erythema, oedema, or irritation.

S.NO	FORMULATION	IRRITANCY EFFECT	ERYTHEMA	OEDEMA
1	Formulation 1	Nil	Nil	Nil
2	Formulation 2	Mild irritation	Nil	Nil
3	Formulation 3	Nil	Nil	Nil
4	Formulation 4	Nil	Nil	Nil
5	Formulation 5	Mild irritation	Nil	Nil

Table no.6: Irritancy study observations

pH

The findings showed that all five of the formulations—F1H, F2H, F3H, F4H, and F5H—had pH values that were closer to skin pH, indicating that they could be applied to the skin without risk^[31].

S.NO	FORMULATION	pH
1	Formulation 1	6.4±1.15
2	Formulation 2	7.1±0.98
3	Formulation 3	7±1.65
4	Formulation 4	5.9±1.42
5	Formulation 5	7.2±2.05

Table no.7 P^H observation studies

Washability

A small amount of cream was applied to the hand, and it was then washed with tap water to conduct the washability test^[32]. Each of the three formulations was simple to wash.

S.NO	FORMULATION	WASHABILITY
1	Formulation 1	Easily washable
2	Formulation 2	Easily washable
3	Formulation 3	Easily washable
4	Formulation 4	Easily washable
5	Formulation 5	Easily washable

Table no.8 Washability observations

Viscosity

Cream's viscosity was measured at 25 °C using a Brooke field viscometer and spindle number 63 spinning at 2.5 RPM. The findings indicated that the viscosity of all three formulations was suitable^[33].

S.NO	FORMULATION	VISCOSITY
1	Formulation 1	48200
2	Formulation 2	45200
3	Formulation 3	23850
4	Formulation 4	22820
5	Formulation 5	14600

Table no.9 Viscosity observations

Phase Separation

The prepared cream was stored away from light and at a temperature between 25 and 100°C in a closed container.

Phase separation was then observed for a full day. Every alteration in the phase separation was examined. The findings show that none of the three formulations showed signs of phase separation^[34].

S. NO	FORMULATION	PHASE SEPARATION
1	Formulation 1	No phase separation
2	Formulation 2	No phase separation
3	Formulation 3	No phase separation
4	Formulation 4	No phase separation
5	Formulation 5	No phase separation

Table no.10Phase Separation observation table.

Spreadability

The spreadability of the five formulations—F1H, F2H, and F3H—was tested. Of these, F2H had the best spreadability because it took the two slides less time to separate, as stated in the evaluation test description. F2H also performed better than the other two formulations in this regard.

S.NO	FORMULATION	TIME	SPRED ABILITY(g×cm/sec)
1	Formulation 1	10	22.8
2	Formulation 2	7	32.4
3	Formulation 3	15	33.5
4	Formulation 4	10	22.4
5	Formulation 5	7	32.4

Table no.11 Spreadability observation table

Greasiness

Here, the cream was smeared onto the skin's surface, and its oiliness or grease-likeness was assessed. We can conclude from the data that none of the three formulations were greasy.

S.NO	FORMULATION	GREASINESS
1	Formulation 1	Non - greasy
2	Formulation 2	Non - greasy
3	Formulation 3	Non - greasy
4	Formulation 4	Non - greasy
5	Formulation 5	Non - greasy

Table no.12 Greasiness observation table

Compatibility study

It is possible to conclude that the three herbal ingredients—*Morinda Tinctoria*, *Tridax Procumbens*, and their active ingredients—are compatible with one another based on the fact that their IR graphs' active ingredients exhibited appropriate peaks^[35].

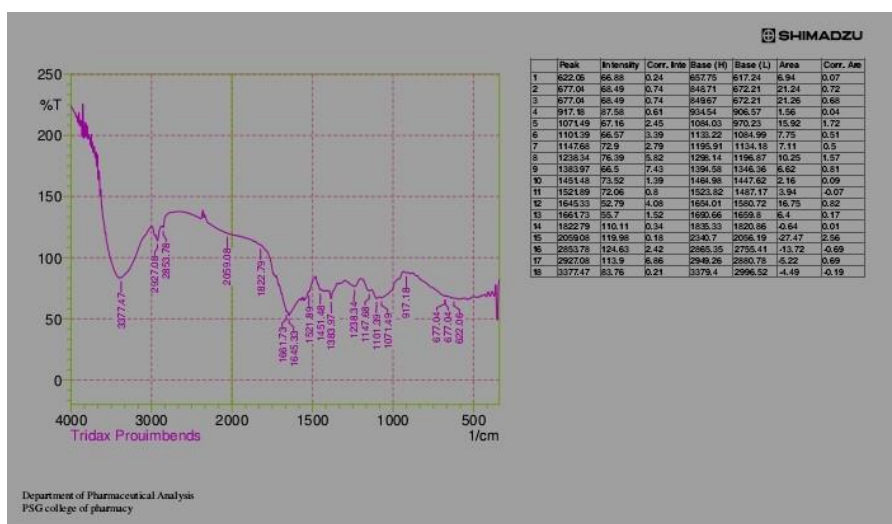


Fig.No.8: FDIR graph of *Tridax Procumbens*

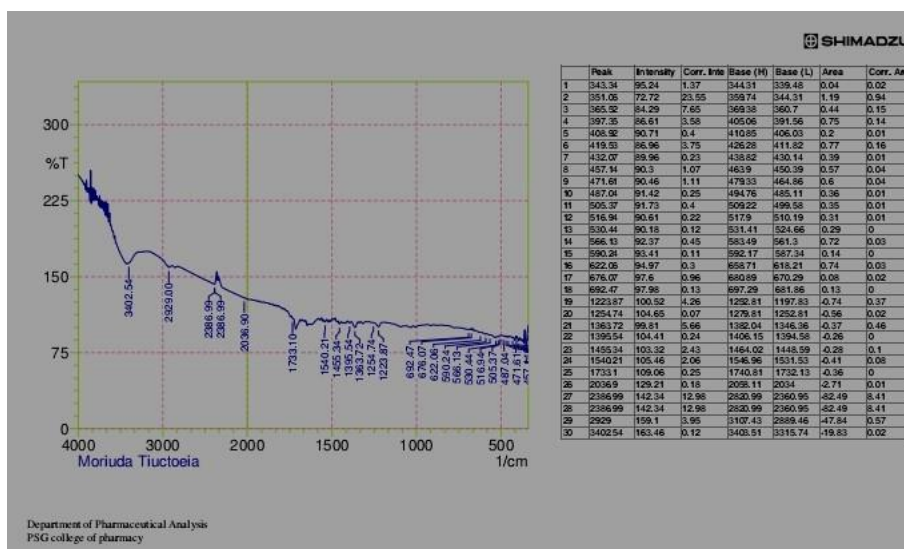


Fig.No.9 :FDIR graph of *Morinda Tinctoria*

SUMMARY AND CONCLUSION

We use a combination of extracts because we are aware that using just one herbal remedy will not provide effective results.

The goal of the current study was to create an anti-inflammatory herbal cream with active ingredients like *Tridax Procumbens* and *Morinda Tinctoria*.

Numerous pharmacological investigations demonstrate the numerous pharmacological activities of *Tridax Procumbens* and *Morinda Tinctoria*. It has stronger anti-inflammatory activity, according to the study. Now let's introduce the leaves of *Tridax Procumbens* and *Morinda Tinctoria*.

Spreadability, viscosity, and pH were among the parameters used to evaluate the cream formulation. The F1 formulation performed significantly better than the F2, F3, F4, and F5 formulations. due to its rapid spreadability and good pH level.

In upcoming clinical trials, applying cream containing *Morinda Tinctoria* and *Tridax Procumbens* may have an anti-inflammatory effect; all three of these herbal ingredients demonstrated noteworthy differences in their activities. The formulation F1 was stable at room temperature and is safe for application on skin, according to the results and discussion.



Fig no 10: Inflammese Cream

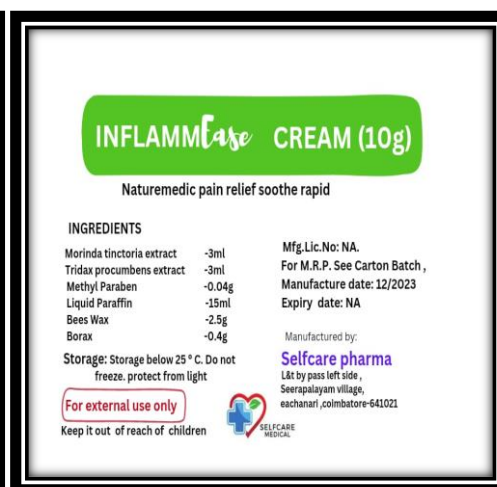


Fig No 11: Label

ACKNOWLEDGMENT

The authors express their sincere gratitude to Mr. S Jeevanandham, the Principal of Sree Abirami College of Pharmacy in Coimbatore, for providing all the excipients and appropriate facilities needed for the formulation.

REFERENCE

1. Schmiedel Y, Zimmerli S. Common invasive fungal diseases: An overview of invasive candidiasis, aspergillosis, cryptococcosis, and Pneumocystis pneumonia. Swiss Medical Weekly, 2016.
2. Fisher M, Hawkins N, Sanglard D, Gurr S. Worldwide emergence of resistance to antifungal drugs challenges human health and food security. Science. 2018;360(6390):739-742.
3. Urban K, Chu S, Scheufele C, Giesey R, Mehrmal S, Uppal P, et al. The global, regional, and national burden of fungal skin diseases in 195 countries and territories: A ~ 295 ~ Journal of Pharmacognosy and Phytochemistry, cross-sectional analysis from the Global Burden of Disease Study 2017. JAAD International. 2021; 2:22-27.
4. Vallabhaneni S, Mody R, Walker T, Chiller T. The Global Burden of Fungal Diseases. Infectious Disease Clinics of North America. 2016;30(1):1-11.
5. Beck S, Mathison H, Todorov T, Calderon-Juarez E, Kopp O. A Review of Medicinal Uses and Pharmacological Activities of *Tridax procumbens* (L.). Journal of Plant Studies. 2018;7(1):19.
6. Policegoudra R, Chattopadhyay P, Aradhya S, Shivaswamy R, Singh L, Veer V. Inhibitory effect of *Tridax procumbens* against human skin pathogens. Journal of Herbal Medicine. 2014;4(2):83-88.

7. Jhample S, Gajdhane S, Kasabe P, Bhagwat P, Dangde P. Phytochemical screening and in vitro antimicrobial activity of *Tridax procumbens* L. *Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences*. 2015;1(1): 44.
8. Berlin Grace V, Viswanathan S, David Wilson D, Jagadish Kumar S, Sahana K, Maria Arbin E, et al. Significant action of *Tridax procumbens* L. leaf extract on reducing the TNF- α and COX-2 gene expressions in induced inflammation site in Swiss albino mice. *Inflammopharmacology*. 2019;28(4):929-938.
9. Akhtar N, Verma A, Pathak K. Topical Delivery of Drugs for the Effective Treatment of Fungal Infections of Skin. *Current Pharmaceutical Design*. 2015;21(20):2892- 2913.
10. Pimpale A. Formulation and Evaluation of Antibacterial, Antifungal Cream of Garlic Oil. *International Journal of Trend in Scientific Research and Development*. 2018;3(1):849-852.
11. Gameda N, Tadele A, Lemma H, Girma B, Addis G, Tesfaye B, et al. Development, Characterization, and Evaluation of Novel Broad-Spectrum Antimicrobial Topical Formulations from *Cymbopogon martini* (Roxb) W. Watson Essential Oil. *Evidence-Based Complementary and Alternative Medicine*, 2018, 1-16.
12. Joshi R, Badakar V. Chemical Composition and in vitro Antimicrobial Activity of the Essential Oil of the Flowers of *Tridax procumbens*. *Natural Product Communications*. 2012; 7(7): 1934578X1200700.
13. Sarkar S, Saha P, Sultana N. In vitro evaluation of phytochemical components and antimicrobial activity of the methanolic extract of *Tridax procumbens* L. against pathogenic microorganisms. *Journal of Pharmacognosy and Phytochemistry*. 2016;5(5):42-46.
14. Sujitha, R, Sharmila R. Phytochemical Analysis and In vitro Anticancer Activity of *Tridax procumbens* Linn. *World Journal of Pharmaceutical Research*. 2018;7(10):867-878
15. Sumeet Dwivedi, Shailesh Gupta, Formulation and Evaluation of Herbal Gel Containing *Sesbania grandiflora* Poir. Leaf Extract, *Acta Chimica and Pharmaceutical India*, 2012, pp.54-59.
- A. Gupta, Formulation and Evaluation of Topical Gel of Diclofenac Sodium Using Different Polymers, *Drug Invention Today*, 2010, 2(5), pp. 250-253.
16. Yogesh P Talekar, Biswadeep Das, Tania Paul, Evaluation of Wound Healing Potential of Aqueous and Ethanolic Extract of *Tridax procumbens* Linn. In *Wistar Rats* 20.K.R.Khandelwal, Vrunda Sethi, *Practical Pharmacognosy*, Nirali prakashan, 2013, pp. 25.1- 25.7
17. Rajesh B., Saumya Das, Pattanayak Dharmajit, M. Pavani, Formulation Design And Optimization Of Herbal Gel Containing *Albizia lebeck* Bark Extract, *International Journal Of Pharmacy And Pharmaceutical Sciences*, Vol.6, 2014, pp.111-114.
18. Shivprasad Majumdar, Ruchi Dave, Formulation Study of Gel Containing *Pterocarpus santalinus* Extract For Its Anti-inflammatory Activity, *World Journal Of Pharmacy And Pharmaceutical Science*, Vol.2 2013, pp.4951-4964.
19. Megha Patel, Nikunjana A. Patel, Formulation and Evaluation Of Polyherbal Gel For Wound Healing, *International Research Journal Of Research Journal Of Pharmaceuticals*, Vol.01,2011, pp.15-20
20. Mali AS, Karekar P, Yadav AV. Formulation and evaluation of multipurpose herbal cream. *Int J Sci Res*. 2015; 4(11): 1495-1497.
21. Christaki EV, Florou-Paneri PC. Aloe vera: A plant for many uses. *J Food Agric Environ*. 2010; 8(2): 245-249.
22. Bhowmik D, Chiranjib YJ, Tripathi KK, Kumar KS. Herbal remedies of *Azadirachta indica* and its medicinal application. *J Chem Pharm Res*. 2010; 2(1): 62-72.
23. Sah AK, Vijaysimha M, Mahamood M. The tulsi, queen of green medicines: Biochemistry and pathophysiology-a review. *Int J Pharm Sci Rev Res*. 2018; 50(2): 106-114.
24. Viswanathan MV, Unnikrishnan PM, Komatsu K, Fushimi H, Basnet P. A brief introduction to Ayurvedic system of medicine and some of its problems. *Indian J Tradit Knowl*. 2003; 2(2): 159-169.

25. Imhof A, Pine DJ. Stability of nonaqueous emulsions. *J Colloid Interface Sci.* 1997; 192(2): 368-374.
26. Bleckmann A, Kropke R, Schneider G, Beiersdorf AG. Preparation of the w/o emulsion type with an increased water content, additionally comprising one or more alkylmethicone copolyols and/or alkyltrimethicone copolyols, and cationic polymers. US patent application. 2021.
27. Kapoor S, Saraf S. Formulation and evaluation of moisturizer containing herbal extracts for the management of dry skin. *Pharmacog J.* 2010; 2(11): 409-417.
28. Ashara K, Soniwala MM, Paun J, Chawda J. Importance of trituration technique on preparation and evaluation of cold cream. *Inventi Rapid Pharm Tech.* 2013: 1-2.
29. Gupta N, Dubey A, Prasad P, Roy A. Formulation and evaluation of herbal fairness cream comprising hydroalcoholic extracts of *Pleurotus ostreatus*, *Glycyrrhiza glabra* and *Camellia sinensis*. *Pharma Bio Sci J.* 2015: 40-45.
30. Rignall A. ICHQ1A (R2) stability testing of new drug substance and product and ICHQ1C stability testing of new dosage forms. *ICH quality guidelines: An implementation guide.* 2017.
31. Meenakshi S, Raghavan G, Virendra N, Kumar A, Shantha M. Antimicrobial, wound healing and antioxidant activity of *Plagiochasma appendiculatum* Lehm. *Journal of Ethnopharmacology.* 2006; 107:67–72.
32. Priya KS, Gnanamani A, Radhakrishnan N, Babu M. Healing potential of *Datura alba* on burn wounds in albino rats. *Journal of Ethnopharmacology.* 2002; 83:193-199.
33. Fabio Carmona, Ana Maria, Soares Pereira. Herbal medicines: old and new concepts, truths and misunderstandings. *Brazilian Journal of Pharmacognosy.* 2013; 23(2):379-385.
34. Koehn FE, Carter GT. The evolving role of natural products in drug discovery. *Nature Review Drug Discovery.* 2005; 4 (3):206-22