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FORMULATION AND IN-VITRO EVALUATION OF POLYHERBAL CREAM FOR THE TREATMENT OF PSORIASIS

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ABSTRACT

A long-term autoimmune skin condition called psoriasis can result in scaly patches on the skin, which can be extremely uncomfortable and embarrassing for the patient. Herbal medicines have become more well-liked as an alternative or complementary therapy for psoriasis because traditional treatments usually have limits. The objective of this study was to formulate and evaluate the efficacy of a polyherbal cream for the treatment of psoriasis made from a combination of herbal extracts, including Terminalia chebula, Cassia tora, Ocimum sanctum, and Cynodondactylon. After making the cream according to a set procedure, we assessed its physical and chemical characteristics. According to the research, the polyherbal cream had sizable anti-inflammatory and antioxidant effects, both of which are crucial for the effective management of psoriasis. In conclusion, our results indicate that a polyherbal cream including extracts of Terminalia chebula, Cassia tora, Ocimum sanctum, and Cynodondactylon might be an effective alternative or complementary therapy for the treatment of psoriasis. To confirm the cream's long-term safety and effectiveness, more clinical trials are required.

Keywords: Polyherbal, Cream, Antifungal, Anti-inflammatory, Psoriasis.

INTRODUCTION

Millions of individuals across the world suffer from the chronic autoimmune skin condition known as psoriasis. The growth of red, scaly areas on the skin that can be itchy, unpleasant, and embarrassing for the sufferer characterises the disorder. Topical corticosteroids and immunosuppressive drugs are two common therapies for psoriasis, however they have some possible adverse effects and are not always effective. Consequently, there has been an increase in interest in the use of herbal treatments for the treatment of psoriasis, either as an alternative or supplementary therapy.[1,2]

The topical treatment for psoriasis known as polyherbal creams has showed encouraging effects. These creams have the benefit of including several therapeutic ingredients that combine to offer superior efficacy, less side effects, and increased patient compliance. As a result, research into the creation of a polyherbal cream for the treatment of psoriasis is exciting[3,4].

In this work, we design a polyherbal cream for the treatment of psoriasis and assess its efficacy. The cream will be created using a standardised process, and both its physical and chemical qualities will be assessed. The cream contains herbal extracts from Terminalia chebula, Cassia tora, Ocimum sanctum, and Cynodondactylon, which have historically been used to treat skin disorders[5,6,7,8].

The Southeast Asian tree Terminalia chebula, often known as Haritaki, has been used for thousands of years in Ayurvedic medicine to treat a variety of conditions, including skin disorders. In animal models, the extract of Terminalia chebula has been demonstrated to have anti-inflammatory and antioxidant effects and to lessen the severity of psoriasis symptoms. Annual legume Cassia tora, often referred to as Sickle Senna, is indigenous to Asia and Africa. Chinese medicine has long employed Cassia tora seeds to treat skin conditions. It has been demonstrated that the anti-inflammatory and antibacterial characteristics of the Cassia tora extract can lessen the

swelling and scaling brought on by psoriasis.

A medicinal herb indigenous to the Indian subcontinent, Ocimum sanctum is also referred to as Holy Basil or Tulsi. Traditional Ayurvedic treatments for psoriasis and other skin conditions include the use of the leaves of Ocimum sanctum. Ocimum sanctum extract has been demonstrated to lessen the inflammation and itching related to psoriasis. It also contains anti-inflammatory, antioxidant, and immunomodulatory activities. A perennial grass that is indigenous to Africa, Asia, and Australia is referred to as Bermuda grass and is called Cynodondactylon. Animal studies have revealed that the Cynodondactylon extract lessens the severity of psoriasis symptoms and has anti-inflammatory and antioxidant qualities.

The final objective of this study is to offer proof that a polyherbal cream made with the chosen herbal extracts may be an alternate or additional therapy for the treatment of psoriasis. The results of the study will help in the creation of innovative, patient-friendly, and safe psoriasis therapy choices. Different substances with anti-inflammatory, antioxidant, and immunomodulatory effects are included in the four herbal extracts that were utilised to make the cream and may help to lessen psoriasis symptoms. It is thought that by mixing these extracts into a polyherbal cream, the treatment for psoriasis will be more effective overall.

MATERIAL AND METHOD

Table no1: Material and method

Sr. no.	Material	Supplier
1.	*Cassia Tora*	Amsar private limited
2.	*Cynodondactylom*	Amsar private limited
3.	*Occimum sanctum*	Amsar private limited
4.	*Terminalia chebula*	Amsar private limited
5.	White bees wax.	Analab fine chemicals, Mumbai.
6.	Liquid paraffin.	Analab fine chemicals, Mumbai.
7.	Borax.	Analab fine chemicals, Mumbai.
8.	Methylparaben.	Analab fine chemicals, Mumbai.
9.	Propylparaben.	Analab fine chemicals, Mumbai.

Equipment

Table no 2: Equipment used

Sr. no.	Equipment	Production Company
1.	Electronic balance	AX 200 Shimadzu, Japan.
2.	UV-Visible spectrometer	Shimadzu, UV1700, Japan.
3.	PH meter	Hanna instruments.
4.	Sonicator	Lag enrich electronics Pvt. Ltd, Vasai.
6.	Franz diffusion cell	Fabricated.
7.	PhotoStability chamber	Biomedia.
8.	Brookfield Viscometer	LVDV-2.

Cream formulation

INGREDIENT	F1	F2	F3	F4	F5	F6	F7	F8	F9
Terminalia chebula extract	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm
Cassia tora extract	0.3 gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm
Occimum	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm	0.3gm

sanctum extract									
Cynodont dactylon extract	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm	0.2gm
Beeswax	1.3gm	1.3 gm	0.9 gm	1.15 gm	1 gm	1.15 gm	1 gm	1.3 gm	1.15 gm
Liquid parafin	13ml	10 ml	11.5 ml	11.15 ml	10 ml	9.3 ml	13 ml	11.5 ml	13.6 ml
Borax	0.08gm	0.08gm	0.08gm	0.08gm	0.08gm	0.08gm	0.08gm	0.08gm	0.08gm
methylparaben	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm
propylparaben	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm	0.004gm
Rosewater	1ml	1ml	1ml	1ml	1ml	1ml	1ml	1ml	1ml
water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation of herbal antifungal cream

Organoleptic evaluation

Additional organoleptic tests were performed on the antifungal cream formulation to assess factors like colour, texture, homogeneity, and foreign particles. Visual examination can be used to determine the cream's colour, texture, and homogeneity. Diffused light was utilised to look for foreign particles in a tiny sample of cream that was spread on a glass slide. [9,10,11]

Measurement of pH

With the aid of a digital PH metre, the PH of herbal cream is measured. 50ml of distilled water and 2gm of cream were dissolved, then left to sit for two hours. Prior to use, the pH metre was calibrated using the recommended pH 4 and pH 7 buffer solutions. For the cream, three separate PH determinations are made.[12,13]

Spreadability

The sample was sandwiched between two slides to achieve uniform thickness, which was then used to test the spreadability of the herbal cream. The amount of time necessary to separate the two slides can be used to determine spreadability. Improved Spreadability was demonstrated by a shorter time required for the separation of cream onto two slides. Spreadability, which was determined using the formula below, is what allows cream formulations to be applied to the skin surface easily.[14,15]

S=ML/T
where
S=Spreadability,
M=Weight connected to the higher slide,
L=Length of glass slides, and
T=Total time needed to separate the slides.

Viscosity

A Brooke field viscometer and concentric cylinder spindle #4 were used to measure the herbal cream's viscosity. A viscometer was used to measure the viscosity of cream, which was dipped into it. Readings were taken at a temperature of 25 °C and at 60 RPM using Brooke field viscometer spindle No. 04[16].

Particle size of Cream:

Characterization of Optimized Formulations:

This investigation was conducted for each of the optimised batches of gels made from carbopol 934, and it looked at globule size and its dispersion in cream. Malvern zetasizer measurements of globule size and distribution were made. Purified water was used to dissolve a 1.0 gramme sample, which was then stirred to achieve homogeneous dispersion. The photocell of the zetasizer received a sample injection. It was determined the distribution and mean globule diameter[17].

Drug content :

Scale the Cream In a 100 ml volumetric flask with 15 ml of methanol, 10 mg of the drug equivalent was added. After stirring for 30 minutes, the remaining volume was filled up with phosphate buffer, and the necessary dilutions were made. A 0.45 m filter was used to filter the final solution. A spectrophotometric analysis was used to determine the solution's absorbance at 268 nm.[18,19]

Drug diffusion test

Franz diffusion cells with cellophane membranes are used to conduct the drug diffusion for all 9 batches. The donor compartment and the receiver compartment are both present in a Franz diffusion cell. A cellophane membrane is positioned between the two chambers. A Franz diffusion cell with a receptor compartment was used for in-vitro drug release experiments. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4 when the prepared cream was placed on the cellophane membrane. The receptor compartment's solution was constantly and continuously agitated using magnetic beads while the entire assembly was fixed on a hot plate magnetic stirrer. At 50 RPM at 37°C+0.5°C, a Franz diffusion cell was used to study the in vitro drug release from cream. As a dissolving medium, phosphate buffer was utilised. Every predetermined amount of time, 1 ml of the dissolution medium was removed and replaced with new dissolution. At regular intervals, the sample was taken out and examined by a UV-spectrophotometer to determine whether the medication was present at 246 nm and 263 nm[20].

Wash ability

A little amount of the herbal cream formulation was put to the skin to test its ability to be easily washed off with water[21].

Irritancy test

A 1 cm2 portion of the left hand's dorsal surface was marked on the hand to conduct an irritancy test. The area in question was then treated with a herbal cream formulation, and the passing of time was noted for up to 24 hours. Results from routine checks for erythema and irritability on a specific location were reported[22,23,24].

Freeze and thaw test

Five times were used to execute the freeze and thaw test on the herbal cream sample. The cream was chilled in a refrigerator and then brought to room temperature. The effect was seen by visual inspection at 52 ºc in the refrigerator and 30 ºc to 35 ºc at ambient temperature[25].

After feel

The herbal-formulated cream sample was evaluated for the after-feel test by slipperiness, emolliency, and the quantity of residue left after the application of the cream. The results were reported, and the outcome was observed by visual observation[26].

Accelerated stability

The resulting herbal cream formulation was tested for accelerated stability at temperatures of 200°C and 400°C for 30 days after being placed in a stability chamber. The cream's appearance, pH, homogeneity, spreadability, viscosity, after-feel, washability, and irritation were all examined over the course of 30 days while the formulations were stored at room temperature[27].

Antimicrobial activity

By using the Cup plate method, the Cup plate method was used to compare the antifungal activity of the optimised batch of the formulation to the antifungal formulation that was commercially available. Candida albicans was the culture employed, and an agar well diffusion antimicrobial test was run. It is sabouraud dextrose agar that is utilised. A sterile Petri plate was filled with prepared nutrients, and the nutrients were left to set. Then, a nichrome wire loop was used to distribute bacterial cultures. The holes were drilled 4 mm deep with a 6 mm diameter sterile cork borer. The optimised batch of gel was then added in increments of 0.5 gm to these holes. 48 hours of incubation on the plates took place at 27 °C. The zone of inhibition (diameter in mm) formed, if any, for fungi was then assessed for the specific drug with each fungal strength.

Results

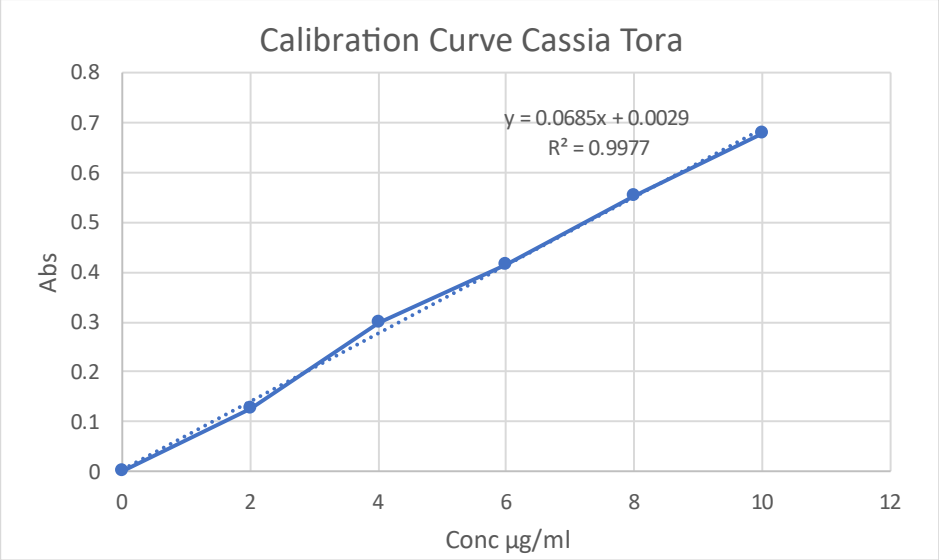


Figure no1 :UV calibration curve of *Cassia tora*extract

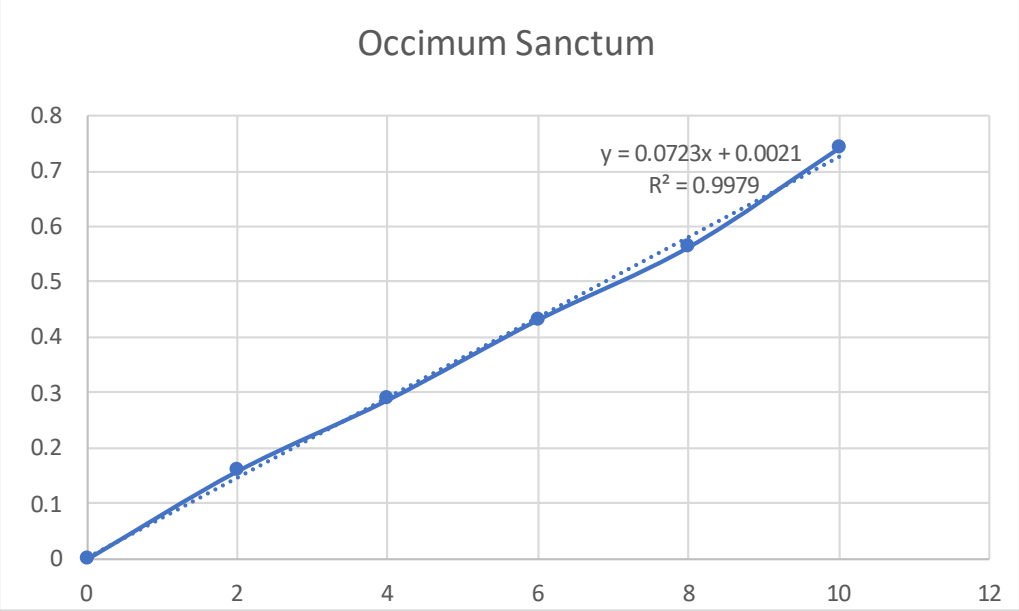


Figure no 2 :UV calibration curve of *Occimum Sanctum* extract

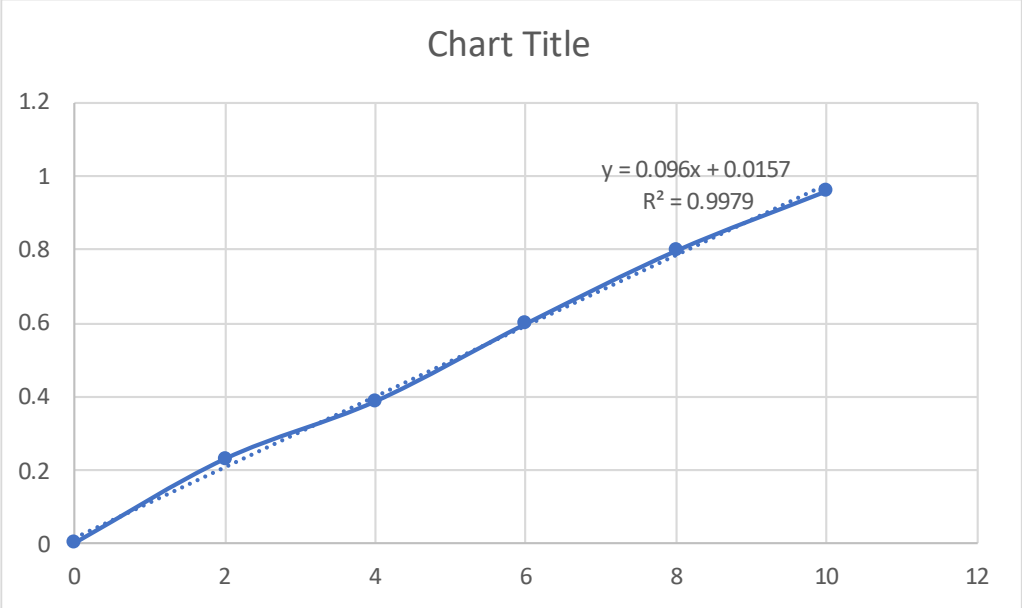


Figure no 3 :UV calibration curve of *Terminalia chebula*extract

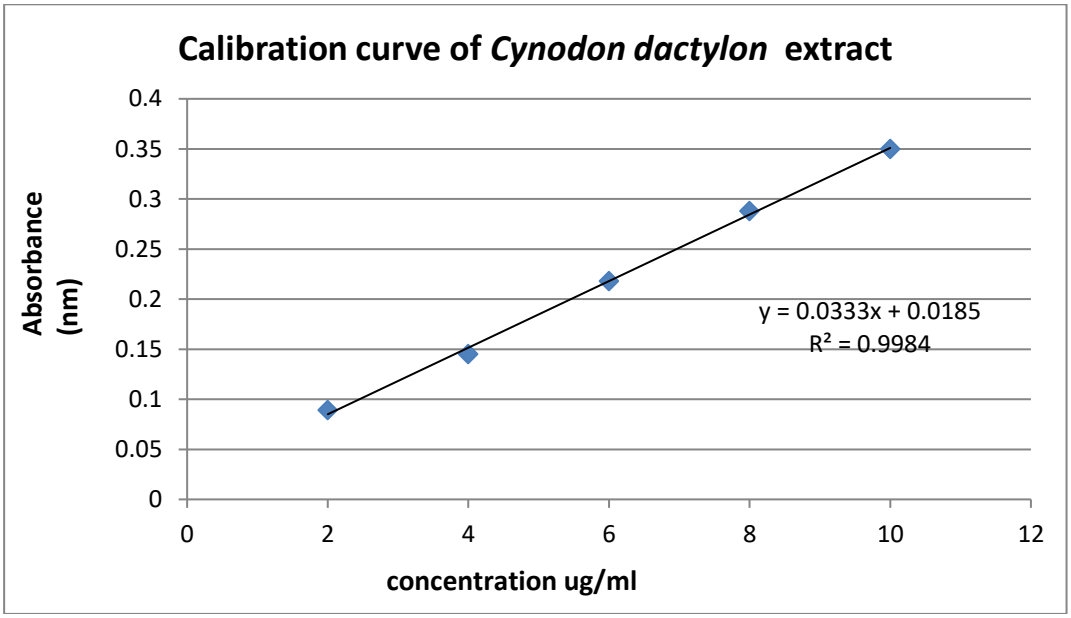


Figure no 4: UV calibration curve of *Cynodondactylon*extract

FT-IR analysis

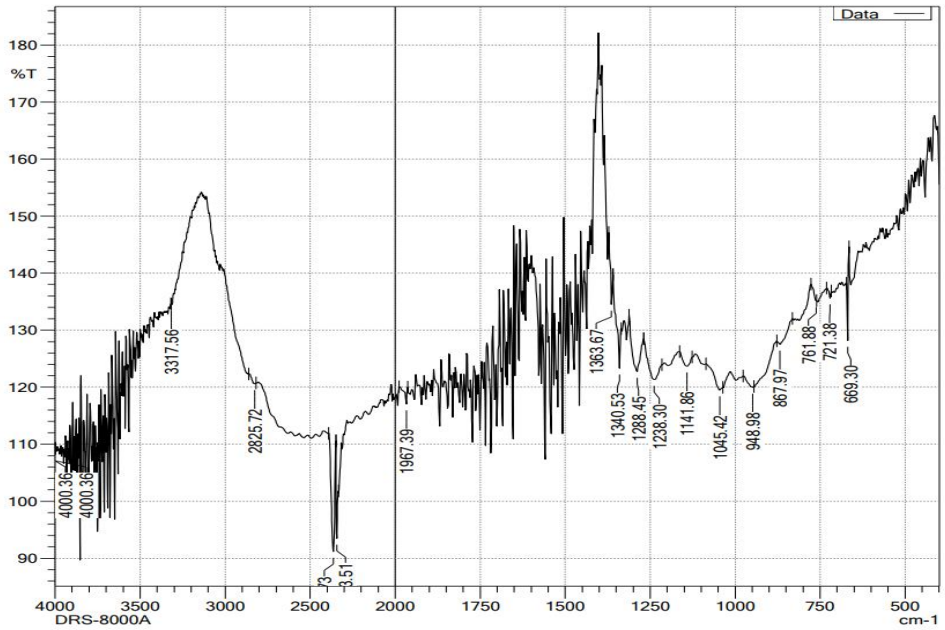


Figure no 5 :FT-IR of Cassia tora

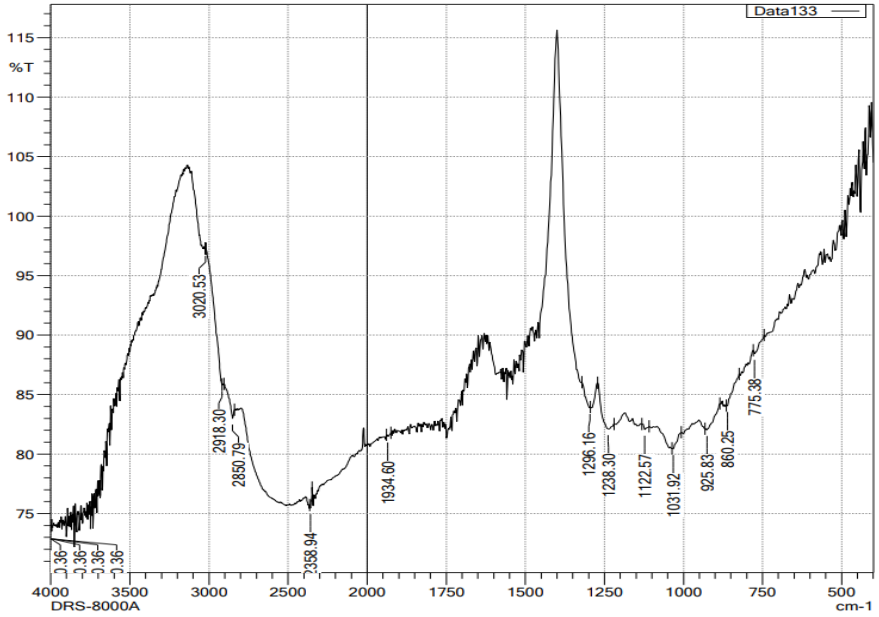


Figure no 6 :FT-IR of *Occimum Sanctum*

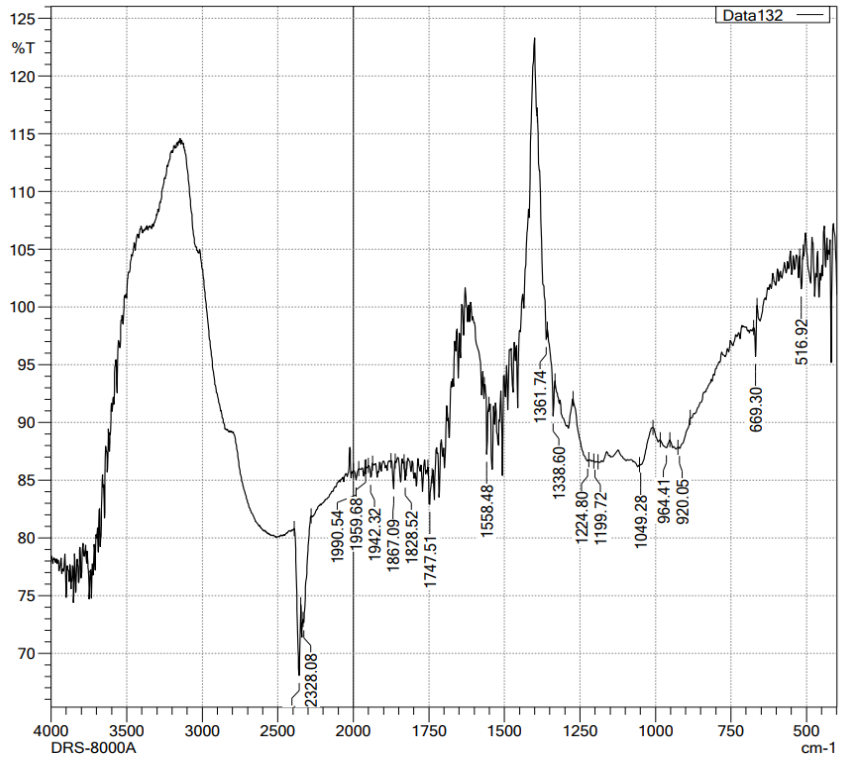


Figure no 7 :FT-IR of *Terminalia chebula*

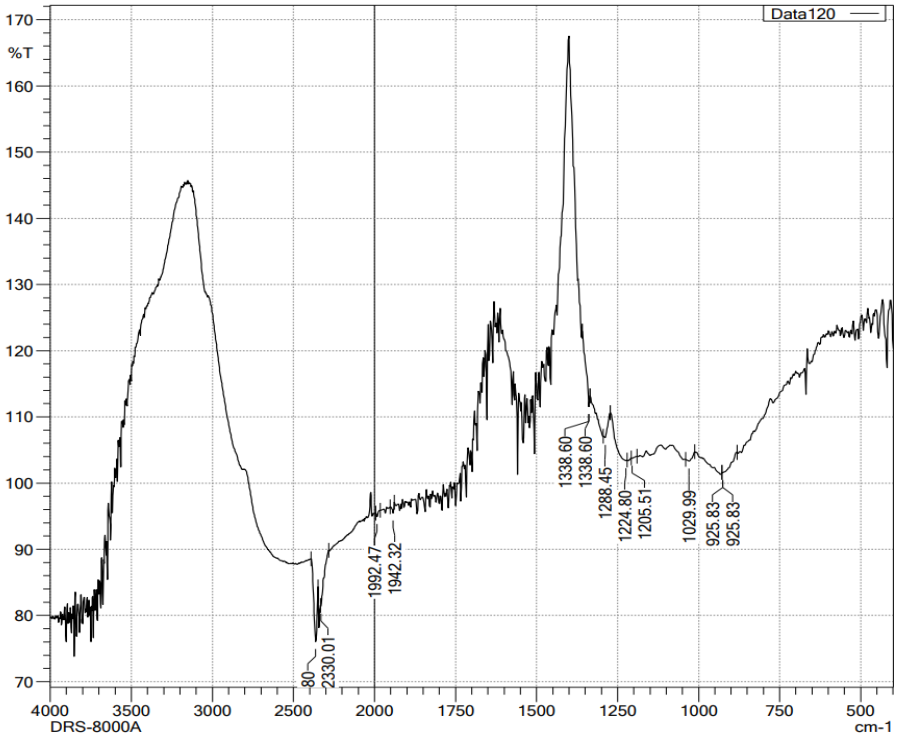


Figure no 8 :FT-IR of *Cynodondactylon*

Organoleptic evaluation

Table no 3: Organoleptic evaluation

Formulation no.	Color	Texture	Homogeneity	Foreign particles
Batch no. F1	Dark brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F2	Dark brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F3	Dark brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F4	**Brownish**	**Smooth**	**Excellent**	**Free from foreign Particles**
Batch no. F5	Brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F6	Brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F7	Brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F8	Faint brownish	Smooth	Excellent	Free from foreign Particles
Batch no. F9	Brownish	Smooth	Excellent	Free from foreign Particles

Measurement of pH

Table no 4 : Measurement of pH

Formulation no.	Observed PH
Batch no. F1	6.3
Batch no. F2	5.7
Batch no. F3	5.9
Batch no. F4	**6.5**
Batch no. F5	6.1
Batch no. F6	5.7
Batch no. F7	6.4
Batch no. F8	5.6
Batch no. F9	6.2

Spreadability

Table no 5 : Spreadability

Formulation no.	Observed Spreadability
Batch no. F1	2.14cm
Batch no. F2	2.23cm
Batch no. F3	2.22cm
Batch no. F4	**3cm**
Batch no. F5	2.11cm
Batch no. F6	2.43cm

Batch no. F7	2.04cm
Batch no. F8	2.33cm
Batch no. F9	1.99cm

Viscosity

Table no 6 : Viscosity

Formulation no.	Observed viscosity
Batch no. F1	14149cp
Batch no. F2	15269cp
Batch no. F3	15843cp
Batch no. F4	**16112cp**
Batch no. F5	140520cp
Batch no. F6	14039cp
Batch no. F7	15612cp
Batch no. F8	15610cp
Batch no. F9	15515cp

Particle size of Cream

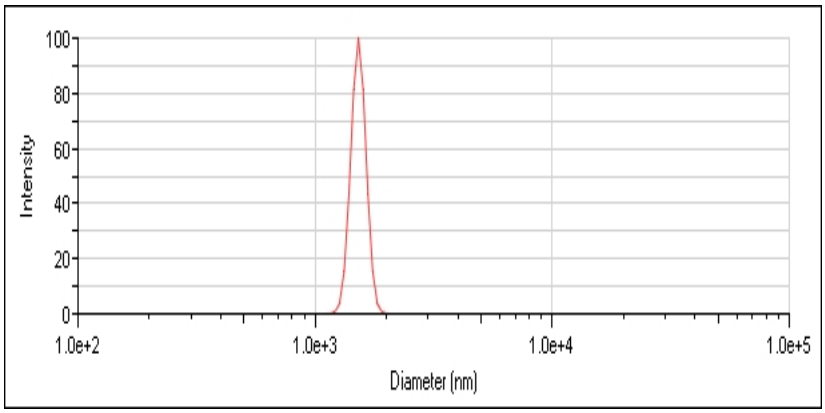


Figure no 9 : Particle size of optimized formulation.

Wash ability

Table no 7 : Wash ability

Formulation no.	Observed washability
Batch no. F1	Easily washable
Batch no. F2	Easily washable
Batch no. F3	Easily washable
Batch no. F4	Easily washable
Batch no. F5	Easily washable
Batch no. F6	Easily washable
Batch no. F7	Easily washable

Batch no. F8	Easily washable
Batch no. F9	Easily washable

Drug content

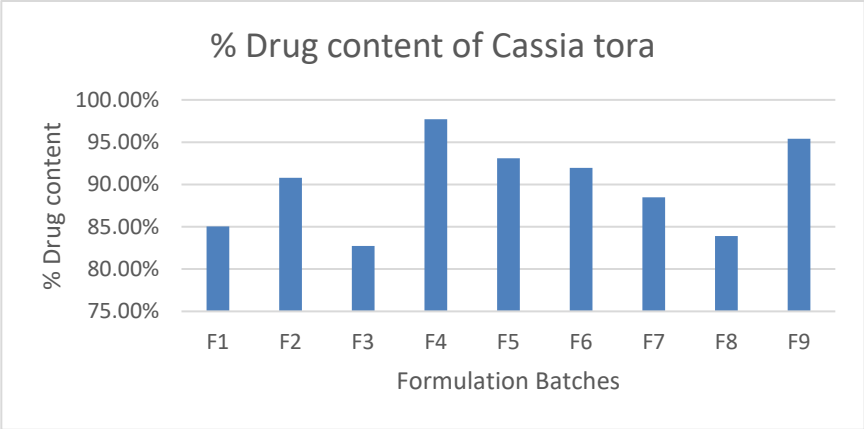


Figure no10: % Drug content Cassia tora

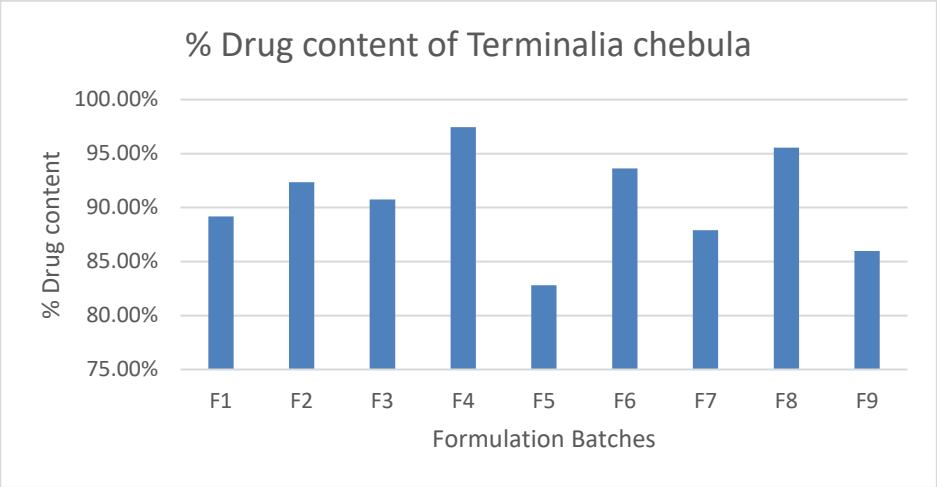


Figure no11: % Drug content Terminalia chebula

Occimum Sanctum

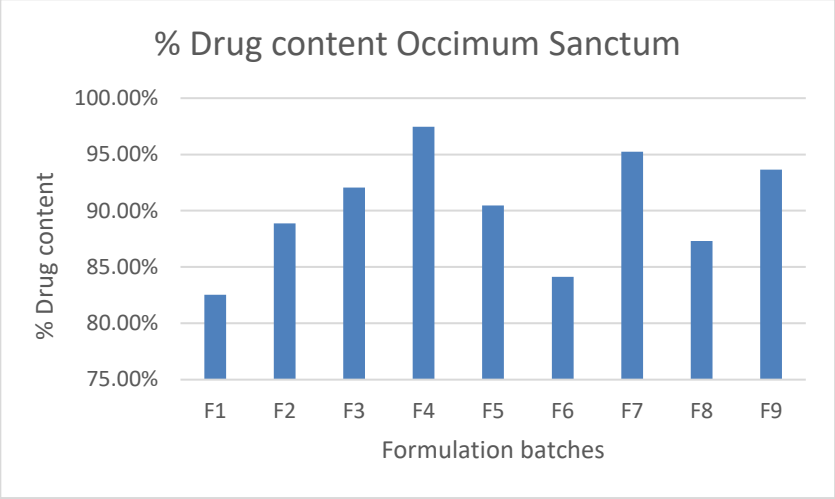


Figure no 12: % Drug content Occimum Sanctum

Cynodondactylon

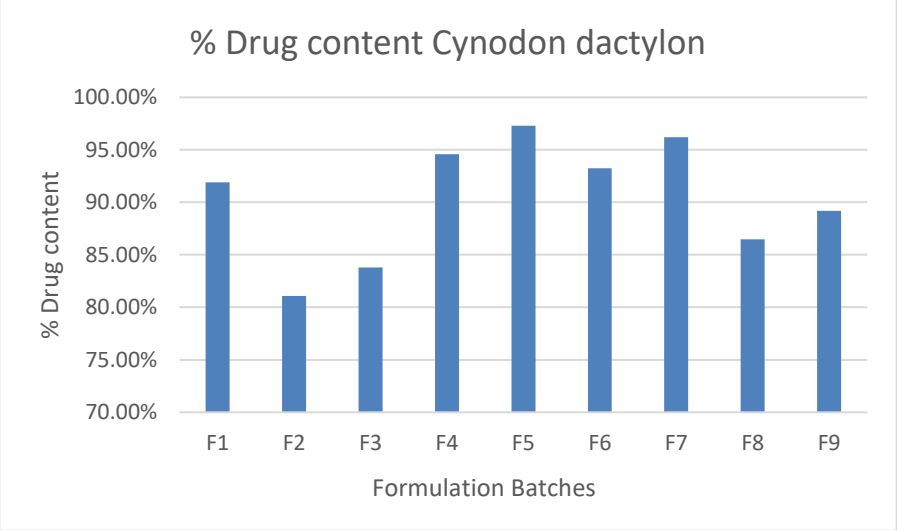


Figure no 13: % Drug content of Cynodondactylon

% Drug release

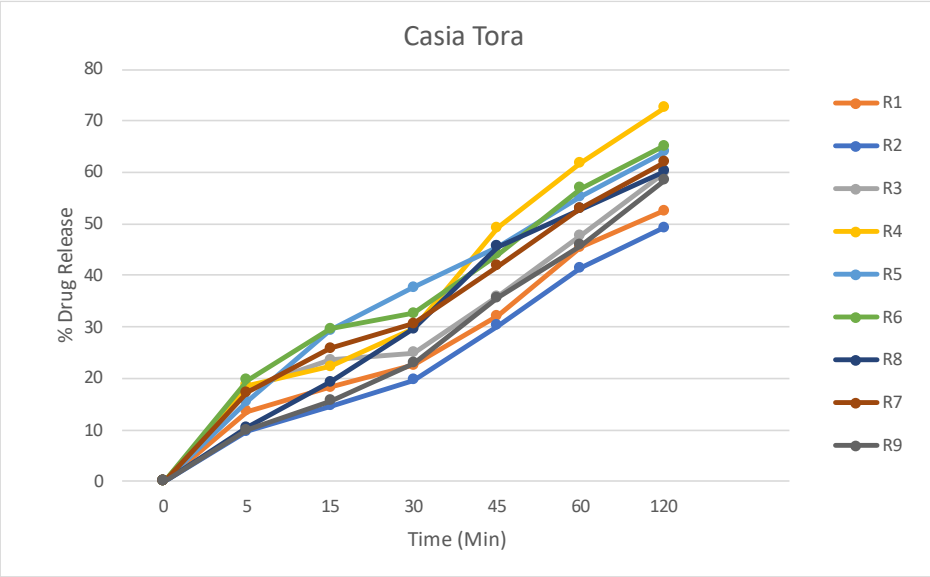


Figure no 14: % Drug release of Cassia tora extract

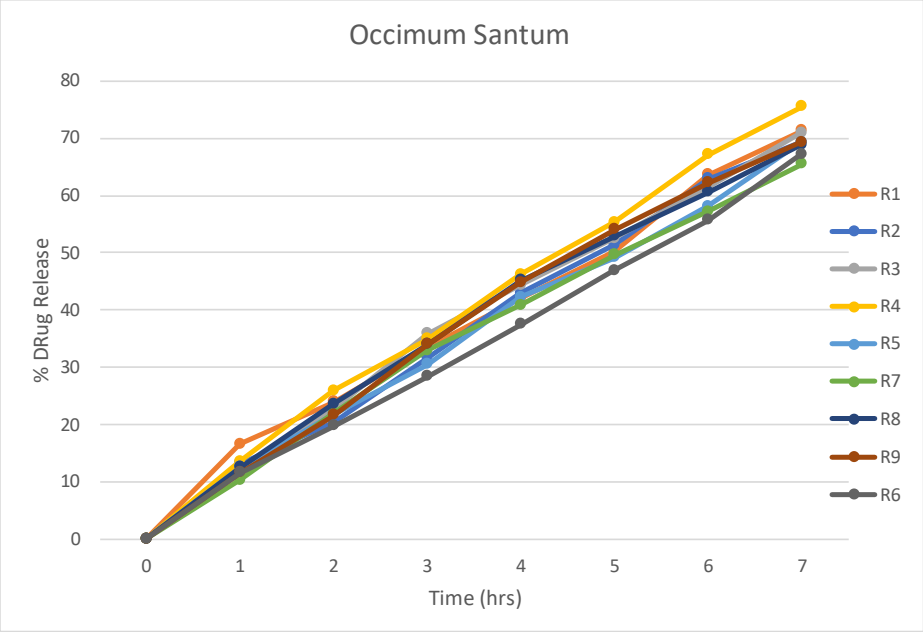


Figure no 15 :% Drug release of *Occimum sanctum* extract

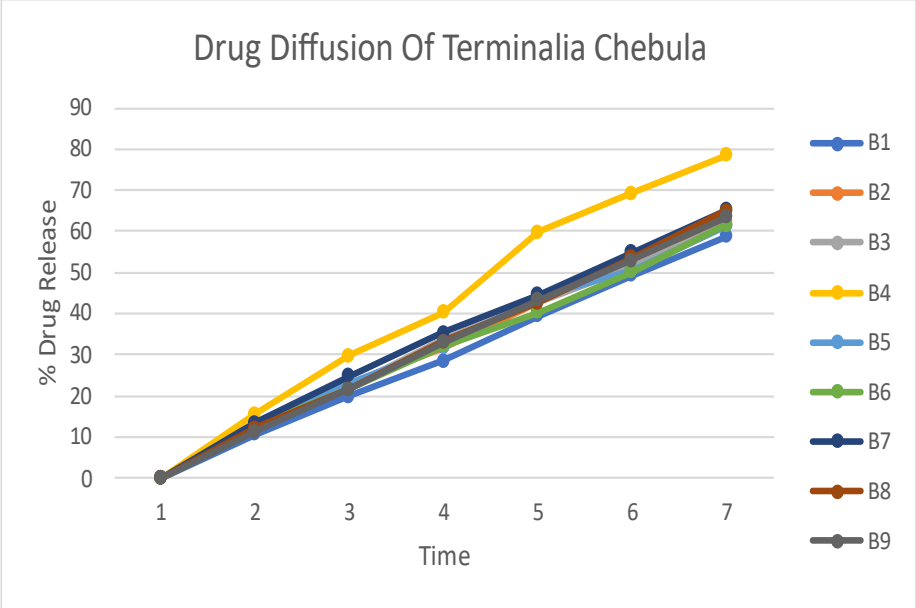


Figure no 16 :% Drug release of Terminalia chebula extract

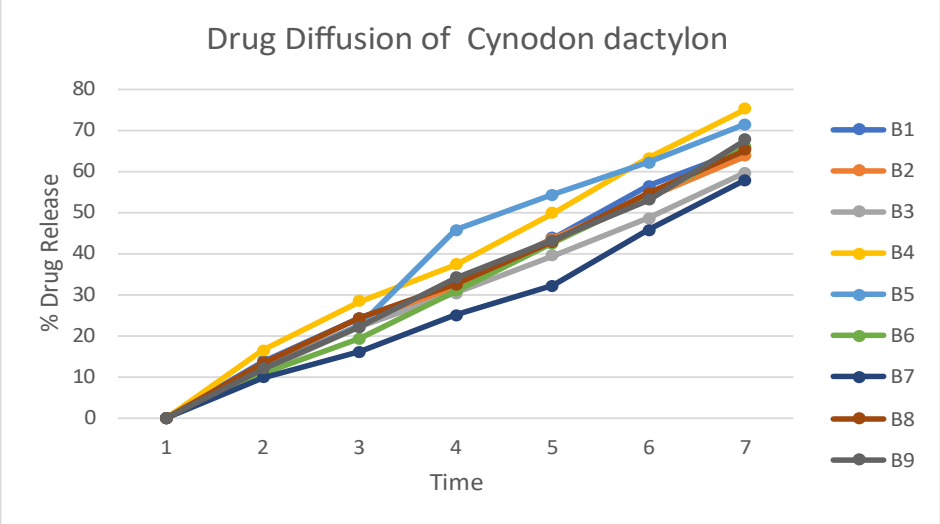


Figure no 17: % Drug release of Cynodondactylon extract

Irritancy test

Table no 9 : Irritancy test

Formulation no.	Irritancy test
Batch no. F1	No irritation
Batch no. F2	No irritation
Batch no. F3	No irritation
Batch no. F4	No irritation
Batch no. F5	No irritation
Batch no. F6	No irritation

Batch no. F7	No irritation
Batch no. F8	No irritation
Batch no. F9	No irritation

Freeze and thaw test

Table no 10: Freeze and thaw test

Formulation no.	Freeze and thaw test
Batch no. F1	Passes
Batch no. F2	Passes
Batch no. F3	Passes
Batch no. F4	Passes
Batch no. F5	Passes
Batch no. F6	Passes
Batch no. F7	Passes
Batch no. F8	Passes
Batch no. F9	Passes

After feel test

Table no 11 : After feel test

Formulation no.	After feel test
Batch no. F1	Emollient
Batch no. F2	Emollient
Batch no. F3	Emollient
Batch no. F4	Emollient
Batch no. F5	Emollient
Batch no. F6	Emollient
Batch no. F7	Emollient
Batch no. F8	Emollient
Batch no. F9	Emollient

Accelerated stability study

Table no 12 : Accelerated stability study

Formulation no.	Accelerated stability study
Batch no. F1	No change was observed.
Batch no. F2	No change was observed.
Batch no. F3	No change was observed.
Batch no. F4	No change was observed.
Batch no. F5	No change was observed.
Batch no. F6	No change was observed.
Batch no. F7	No change was observed.

Batch no. F8	No change was observed.
Batch no. F9	No change was observed.

Antimicrobial activity study

Table no 13 : Antimicrobial activity study

Formulation sample.	Observed Zone of inhibition
Marketed formulation	12 ± 1 mm
Optimized batch F4	15.55± 1.50 mm

HPTLC analysis of extracts

HPTLC analysis of Terminalia chebula extract

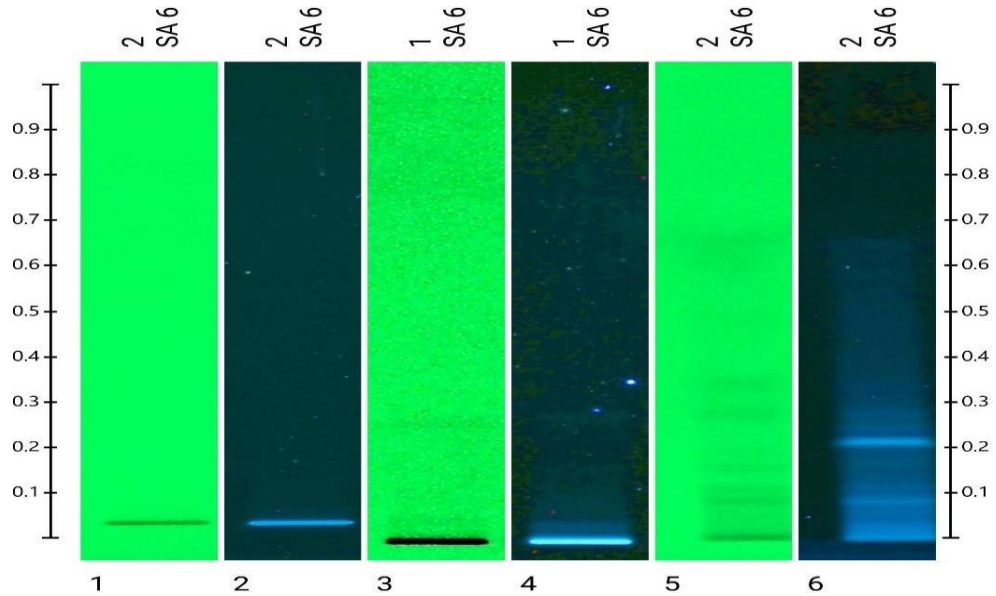


Figure No.18: Photo documentation of Terminalia chebula at 1) Visible 2) 254 nm and 3) 366 nm

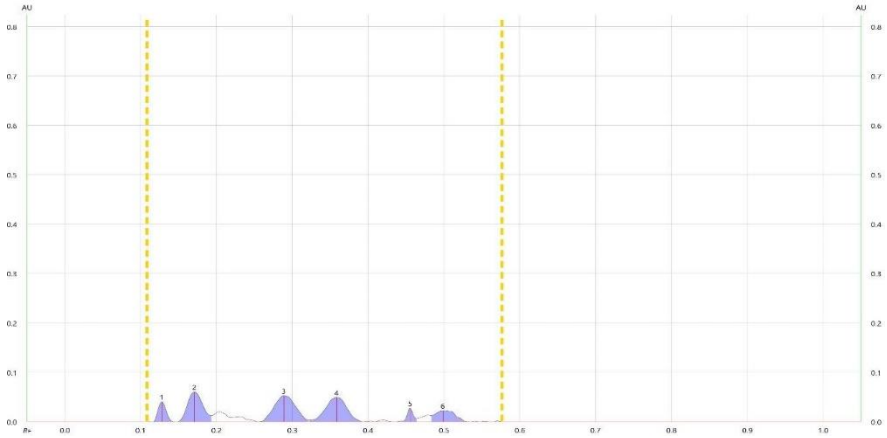
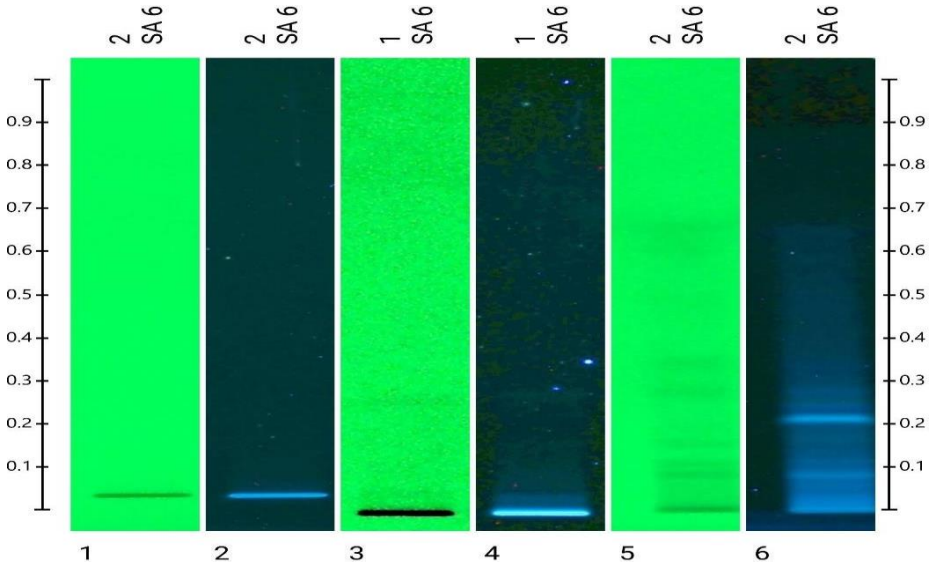


Figure no19: Densitogram of *Terminalia chebula*extract

HPTLC analysis of Ocimum sanctum

Figure no 20 : Photo documentation of Ocimum sanctum at 1) Visible 2) 254 nm and 3) 366 nm



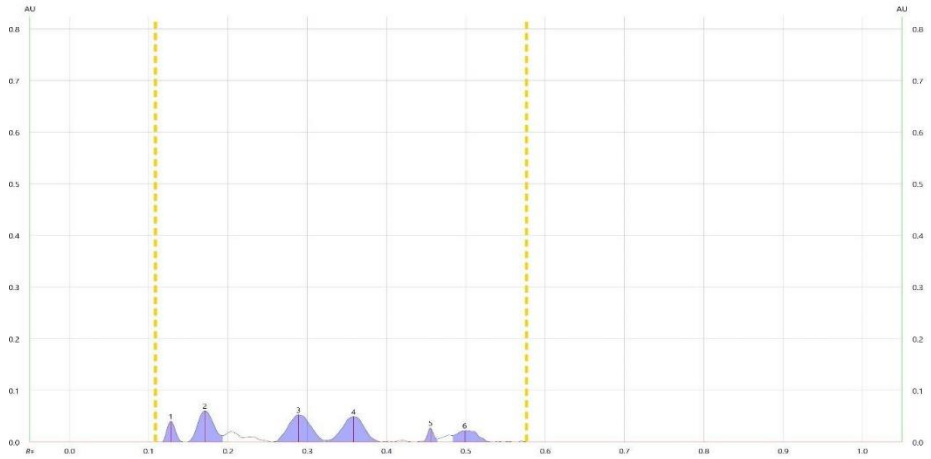
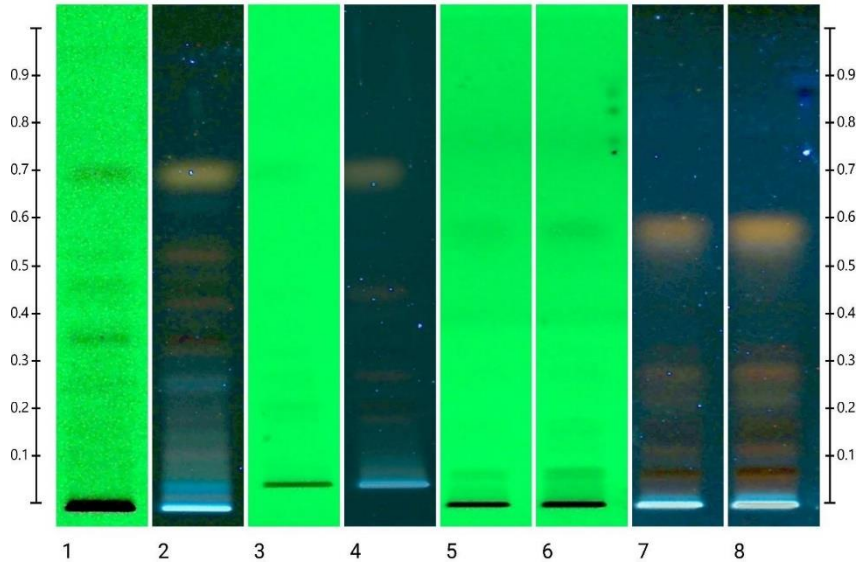


Figure no21 : Densitogram of *Ocimum sanctum* extract

HPTLC analysis of Cassia tora

Figure no 22 : Photo documentation of *Cassia tora* at 1) Visible 2) 254 nm and 3) 366 nm



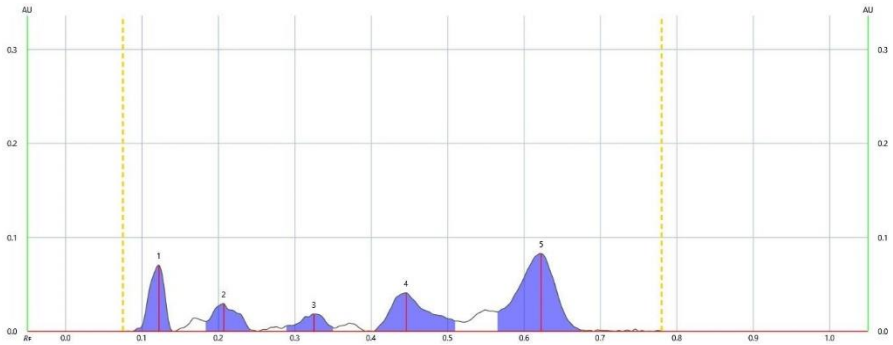


Figure no 23 : Densitogram of *Cassia tora*extract

HPTLC analysis of CynodonDactylon

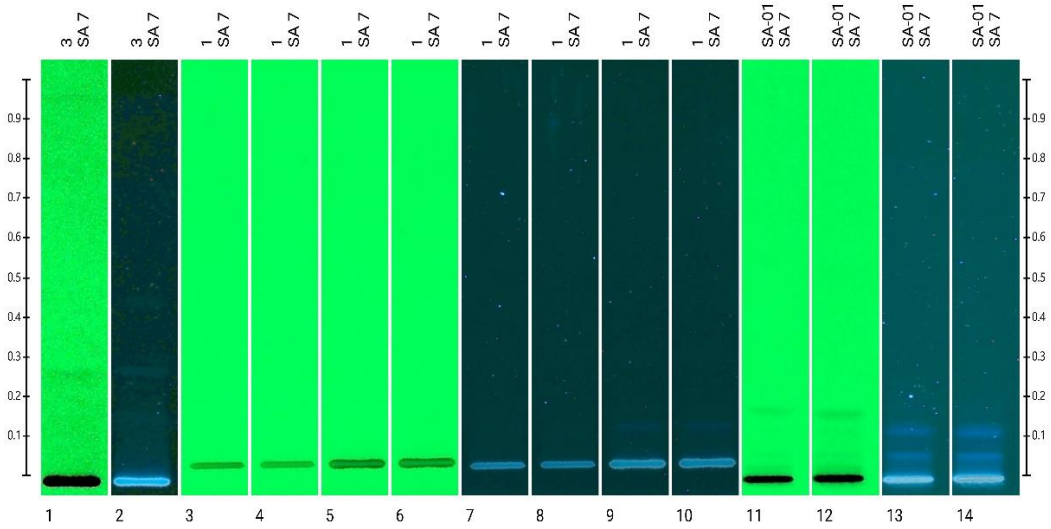


Figure no 24 : Photo documentation of Cynodondactylon at 1) Visible 2) 254 nm and 3) 366 nm

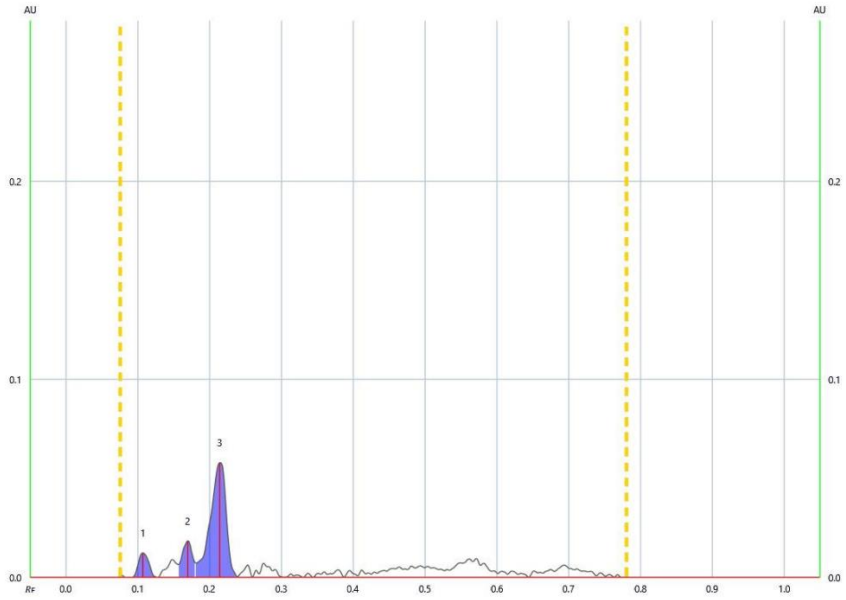


Figure no 25: Densitogram of *Cynodondactylon*extract

- **Images of cell activity-**

Table no.14- Effects of compound against L-929 (adherent type of mouse fibroblast cell line) by MTT assay

Sr. no	Sample	Concentration(µg/ml)	OD	Mean	% inhibition	IC 50 (µg/ml))
1	Control		0.899 0.891 0.837	**0.875**		
2	Std. 5 FU	10	0.212 0.201 0.196	**0.203**	76.08	32.07
		40	0.105 0.117 0.125	**0.115**	86.85	
		100	0.078 0.093 0.100	**0.090**	89.71	
3	Sample – F4	10	0.325 0.351 0.310	**0.328**	62.51	38.19
		40	0.289 0.274 0.295	**0.286**	67.31	
		100	0.260 0.259 0.245	**0.254**	70.97	

According to Table, at the different Concentration (10 µg/ml, 100 µg/ml, 100 µg/ml) of Sample – F4 compounds carried out activity against **L-929 (adherent type of mouse fibroblast cell line).** The positive control 5 Flurouracil was used as standard drug. The Sample – F4 showed good activity as compared to standard compound.

Control

Standard 5FU

Sample – F4

Table no. 15 Anti-inflammatory activity of different formulation by Protein denaturation method

Compounds	**Conc.**	**O.D.**	**Mean**	**% inhibition**
Blank		1.50 1.45 1.48	1.47	
Standard (Diclofenac sodium)	1000 µg/ml	0.13 0.14 0.15	0.14	90.47
Samples: B (AB)	1000 µg/ml	0.25 0.26 0.24	0.25	82.99

In conclusion, All Samples B (AB) Were used to carry out in vitro anti-inflammatory activity by using protein denaturation inhibition assay at the concentration 1mg/ml. The all samples showed good anti-inflammatory activity as compared to standard drug (Diclofenac sodium).

CONCLUSIONS

The main purpose of this study is to develop an herbal cream. The efficient selection of medicinal plants and their extract with correct concentration with perfect formulation can show a good medicinal effect on the body and it may increase the potency of drugs and formulation. The use of *Terminaliachebula,Cassia tora , Occimum sanctum* and*Cynodondactylon*herbal cream shows an antifungal effect and all these herbal ingredients showed various activities such as antimicrobial, antibacterial, antiviral, Antiprotozoal, Antihelmintic, Anti-diabetic. The herbal cream formulation is stable at room temperature and can be effectively used against various diseases on the skin.

The presented study of the *Terminaliachebula,Cassia tora , Occimum sanctum* and*Cynodondactylon* extract for the effective management of antifungal diseases might increase penetration of the drug from the affected area that it may show antibacterial activity also, due to the presence of propylene glycol, it may increase the moisturizing effect.

All the evaluations of the cream formulations of the *Terminaliachebula,Cassia tora , Occimum sanctum* and*Cynodondactylon*extract states that the F4 formulation gives comparatively optimum results of drug release, viscosity, spreadability, and pH.

REFERENCES

Bishir,M.*etal.*(2020)‘SleepDeprivationandNeurologicalDisorders’,*BioMedresearchinternational*,2020,p.5764017
.

Bodner,L.,Woldenberg,Y.andBar-Ziv,J.(2003)‘Radiographicfeatures

oflargecysticlesionsofthejawsinchildren',*Pediatric radiology*,33(1),pp.3–6.
Boyczuk, M. P., Berger, J. R. and Lazow, S. K. (1995) 'Identifying a deciduous dentigerouscyst',*Journalofthe AmericanDentalAssociation*,126(5),pp.643–644.
Chandrasekar,R.*etal.*(2020)'Developmentandvalidationofaformulaforobjectiveassessmentofcervicalvertebralbone age',*Progressinorthodontics*,21(1),p.38.
Delbem,A.C.B.*etal.*(2006)'Dentigerouscystsinprimarydentition:reportof2cases',*Pediatricdentistry*, 28(3),pp. 269–272.
Fan, Y. *et al.* (2021) 'Tomentosin Reduces Behavior Deficits and Neuroinflammatory Responsein MPTP-Induced Parkinson's Disease in Mice', *Journal of environmental pathology, toxicologyand oncology: official organ of the International Society for Environmental Toxicology andCancer*,40(1),pp.75–84.
Felicita, A. S. and Sumathi Felicita, A. (2018) 'Orthodontic extrusion of Ellis Class VIII fractureof maxillary lateral incisor – The sling shot method',*The Saudi Dental Journal*, pp. 265–269.doi:10.1016/j.sdentj.2018.05.001.
Gan,H.*et al.*(2019) 'Zingerone induced caspase-dependentapoptosisin MCF-7 cells andprevents7,12-dimethylbenz(a)anthracene-inducedmammarycarcinogenesisinexperimentalrats',*Journalofbiochemicalandmoleculartoxicology*,33(10), p.e22387.
Iatrou, I., Theologie-Lygidakis, N. and Leventis, M. (2009) 'Intraosseous cystic lesions of thejaws in children: a retrospective analysis of 47 consecutive cases', *Oral surgery, oral medicine,oralpathology,oralradiology,andendodontics*,107(4),pp.485–492.
Jones, A. V., Craig, G. T. and Franklin, C. D. (2006) 'Range and demographics of odontogeniccystsdiagnosedinaUKpopulationovera30-yearperiod',*Journaloforalpathology&medicine:official publication ofthe InternationalAssociationofOralPathologists and theAmerican Academy ofOralPathology*,35(8),pp.500–507.
J, P. C. *et al.* (2018) 'Prevalence and measurement of anterior loop of the mandibular canal usingCBCT: A cross sectional study', *Clinical Implant Dentistry and Related Research*, pp. 531–534.doi:10.1111/cid.12609.
Li, S. *et al.* (2019) 'Restorative Effect of Fucoxanthin in an Ovalbumin-Induced Allergic RhinitisAnimal Model through NF-κB p65 and STAT3 Signaling', *Journal of environmental pathology,toxicologyandoncology:officialorganoftheInternationalSocietyforEnvironmentalToxicology andCancer*,38(4),pp.365–375.
Manor, E. *et al.* (2012) 'Cystic Lesions of the Jaws - A Clinicopathological Study of 322 CasesandReviewof theLiterature',*InternationalJournalofMedicalSciences*,pp.20–26.doi:10.7150/ijms.9.20.
Martínez-Pérez, D. and Varela-Morales, M. (2001) 'Conservative treatment of dentigerous cystsin children: A report of 4 cases', *Journal of Oral and Maxillofacial Surgery*, pp. 331–333. doi:10.1053/joms.2001.21006.
Ma,Y.*etal.*(2019)'SesameInhibitsCellProliferationandInducesApoptosisthroughInhibition of STAT-3 Translocation in ThyroidCancerCell Lines (FTC-133)',*Biotechnologyandbioprocess engineering:BBE*,24(4),pp.646–652.
Meara, J. G.*et al.* (1996) 'Odontogenic Keratocysts in the Pediatric Population',*Archives ofOtolaryngology-HeadandNeckSurgery*,pp.725–728.doi:10.1001/archotol.1996.01890190021006.
Miyawaki, S.*et al.* (1999) 'Eruption speed and rate of angulation change of a cyst-associatedmandibular second premolar after marsupialization of a dentigerous cyst',*American journal oforthodontics and dentofacial orthopedics: official publication of the American Association ofOrthodontists, its constituent societies, and the American Board of Orthodontics*, 116(5), pp.578–584.
Mudigonda,S.K.*etal.*(2020)'Non-suturingmicrovascularanastomosisinmaxillofacialreconstruction- a comparative study', *Journal of Cranio-Maxillofacial Surgery*, 48(6), pp. 599–606.
Murakami, A. *et al.* (1995) 'Eruption of an impacted second premolar after marsupialization of alarge dentigerouscyst:casereport',*Pediatric dentistry*,17(5),pp.372–374.
Narayanasamy, R. K. *et al.* (2021) 'Lower pretreatment hemoglobin status and treatment breaksin locally advanced head and neck squamous cell carcinoma during concurrent

chemoradiation',*Indianjournalofcancer*,58(1),pp.62–68.
'Oralpathology:Clinicalpathologiccorrelations(ed3)'(1999)*JournalofOralandMaxillofacialSurgery*,pp.633–634.doi:10.1016/s0278-2391(99)90110-6.
Prabhu, N. T., Rebecca, J. and Munshi,A. K. (1996) 'Dentigerous cyst with inflammatoryetiologyfrom adeciduouspredecessor--reportof acase',*JournaloftheIndianSocietyofPedodonticsandPreventiveDentistry*,14(2),pp.49–51.
Ramakrishnan,M.,Dhanalakshmi,R.and Subramanian,E.M.G.(2019)'Survival rate ofdifferent fixed posterior space maintainers used in Paediatric Dentistry – A systematic review',*The SaudiDentalJournal*,pp.165–172.doi:10.1016/j.sdentj.2019.02.037.
Rubin,D.M.,Vedrenne,D.and Portnof,J.E. (2002)'Orthodontically guided eruption ofmandibular second premolar following enucleation of an inflammatory cyst: case report',*TheJournalofclinicalpediatric dentistry*,27(1),pp.19–23.
Saravanakumar, K. *et al.* (2021) 'Chemical composition, antioxidant, and anti-diabetic activitiesof ethyl acetate fraction of Stachys riederi var. japonica (Miq.) in streptozotocin-induced type 2diabetic mice', *Food and chemical toxicology: an international journal published for the BritishIndustrialBiologicalResearchAssociation*,155,p.112374.
Sathya, S. *et al.* (2020) 'An in vitro study on hexavalent chromium [Cr(VI)] remediation usingironoxidenanoparticlesbasedbeads',*EnvironmentalNanotechnology,Monitoring&Management*,14,p.100333.
Scholl, R. J. *et al.* (1999) 'Cysts and Cystic Lesions of the Mandible: Clinical and Radiologic-Histopathologic Review',*RadioGraphics*, pp.1107–1124.doi:10.1148/radiographics.19.5.g99se021107.
Stoelinga,P.J. (2001)'Long-term follow-upon keratocysts treatedaccordingtoa definedprotocol',*Internationaljournaloforalandmaxillofacialsurgery*,30(1),pp.14–25.
Su, P. *et al.* (2019) 'A ginger derivative, zingerone-a phenolic compound-induces ROS-mediatedapoptosis in colon cancer cells (HCT-116)', *Journal of biochemical and molecular toxicology*,33(12),p.e22403.
Veeraraghavan,V.P.*etal.*(2021)'AComprehensiveandCriticalReviewonEthnopharmacological Importance of Desert Truffles: Terfeziaclaveryi, Terfeziaboudieri, andTirmanianivea',*FoodReviewsInternational*,pp.1–20.
Wahab, P. U. A.*et al.*(2018) 'Scalpel Versus Diathermy in Wound Healing After MucosalIncisions: A Split-Mouth Study',*Journal oforal and maxillofacial surgery: official journal oftheAmerican Association ofOral andMaxillofacialSurgeons*,76(6),pp.1160–1164.
Wang, H. *et al.* (2021) 'Phyllanthin inhibits MOLT-4 leukemic cancer cell growth and inducesapoptosis through the inhibition of AKT and JNK signaling pathway',*Journal of biochemicalandmolecular toxicology*,35(6),pp.1–10.
Wan,J.*etal.*(2020)'AntiatherosclerоticActivityofEriocitrininHigh-Fat-Diet-InducedAtherosclerosis Model Rats',*Journal of environmental pathology, toxicology and oncology:official organ of the International Society for Environmental Toxicology and Cancer*, 39(1), pp.61–75.
Weber, A. L. (1993) 'Imaging of cysts and odontogenic tumors of the jaw. Definition andclassification',*Radiologic clinicsofNorthAmerica*,31(1),pp.101–120.
Wei, W. *et al.* (2021) 'Amelioration of oxidative stress, inflammation and tumor promotion byTin oxide-Sodium alginate-Polyethylene glycol-Allyl isothiocyanate nanocomposites on the 1,2-Dimethylhydrazine induced colon carcinogenesis in rats',*Arabian Journal of Chemistry*, 14(8),p.103238.
Young, C. W., Pogrel, M. A. and Schmidt, B. L. (2007) 'Quality of life in patients undergoingsegmental mandibular resection and staged reconstruction with nonvascularized bone grafts',*Journal of oral and maxillofacial surgery: official journal of the American Association of OralandMaxillofacialSurgeons*,65(4),pp.706–712.
Zhang, C. *et al.* (2020) 'Vicenin-2 Treatment Attenuated the Diethylnitrosamine-Induced LiverCarcinomaandOxidativeStressthroughIncreasedApoptoticProteinExpressioninExperimentalRats',*Journalof environmentalpathology,toxicologyandoncology:officialorgan of the International Society for Environmental Toxicology and Cancer*, 39(2), pp. 113–123.