RESEARCH PAPER

Development And Characterization Of A Topical Film- Forming Gel Containing Polyherbal Extracts

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ABSTRACT
Film forming gels have been used as tissue glues for the closing of operative wounds. The study was based on the development and evaluation of a topical film- forming gel containing polyherbal extracts for treatment of fungal infection. Extraction of the plant materials through cold maceration process using water and chloroform (1:1) solvent was done. After, preliminary phytochemical screening of herbal extract, the pre-formulation study was performed. Solvent casting method was utilized for the formulation of film-forming gel and evaluated for parameters i.e., physical appearance, pH estimation, drug content, spredability, drying time, film formation, film flexibility, film thickness, weight variation, folding endurance, in-vitro release study. The fresh leaves of Azadirachta indica and Ocimum sanctum were collected from the UP east and authenticated from the botanist at BSI, Allahabad with reference no. 2023-24/529. The dried leaves of Azadirachta indica, and Ocimum sanctum were rendered into fine powder and extracted using distilled water and chloroform (1:1) solvent system through cold maceration process. In HPTLC analysis, flavonoids, tannins and terpenoids were predicted. Herbal extracts were found as water insoluble. A. indica leaves extract and O. sanctum leaves extract showed the maximum absorption (λmax) at 257 nm and 320 nm, respectively. In results, the formulated polyherbal extracts based film forming gel showed the optimized film formation & flexibility, pH, film thickness, spreadability, and drying time in F1-F6. The drug content and in-vitro drug release was also found excellent when determined for different time intervals i.e., 0, 0.5, 1, 2, 3, 4, 5, 6, 12, 18, 24 hours. In conclusion, among all the films forming gel, F5 was selected as optimized formulation. Highest in-vitro release was found to be 93.21 % (F5) in 24 hours, which demonstrates a better sustained release formulation..
Keywords: Film forming gel, A. indica, O. sanctum, HPTLC, in-vitro drug release.
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INTRODUCTION

With a surface area of 1.5-2 m^2, the skin is the biggest organ in the body and the most intricate barrier between the biological system and the external environment (Waugh & Grant, 2014). It is composed of three layers: intra-subcutaneous fatty tissue, a dermis that is 250 millimetres thick, and an outer epidermis that is 50 to 150 millimetres thick (Moghimi et al. 2011). The superficial layers of the stratum corneum, which make up the epidermal area, have a special cellular structure that prevents molecules bigger than 500 Da from penetrating and provides physical defence against microbial penetration (Gupta et al. 2012).

At first, the fields of surgery and wound care were the main applications for film making technologies. In order to close surgical wounds, tissue glues such as film forming solutions or gels have been employed (Bajaj et al. 2016). Additionally, it may be utilized for non-medical purposes, such delivering active compounds found in cosmetic items, such as silicone film forming technology used to make ointments and creams (Klykken et al. 2009). Compared to more traditional formulation types, film forming systems have several advantages. They can deliver a unit dose, enhance drug delivery, be applied to large application areas with ease, and minimize product transference losses onto clothing or other people due to their quick drying and absorbing properties (Frederiksen K., et.al. 2015).

Azadirachta indica (neem) belongs to Meliaceae family. It is highly cultivated in tropical & semitropical regions- India, Pakistan, Bangladesh & Nepal. It is a rapidly tree that can reach 20–23 m in height and has a straight trunk with a width of 4-5ft. The leaf is complex, imparipinnate and have 5-15 (leaflets) each. Its fruits are greenish drupes that changes in golden yellow on ripe (Alzohairy, 2016).

Ocimum tenuiflorum belongs to the Lamiaceae family. It has contributed to science from ancient times to the present day in current practices because of its many restorative potentials. Tulsi is a significant symbol of Hindu intellectual traditions. Tulsi is one of the most important plants in Ayurveda. Tulsi is the finest Ayurvedic knowledge tonic for the body and mind, and it may treat a variety of contemporary disorders (Cohen, 2014).

MATERIALS AND METHODS

Materials

Table 1. List of drug & excipients

S.N.	Materials	Category
	Azadirachta indica	Plant Extract
	Ocimum sanctum	Plant Extract

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	Eudragit RS PO	Co-polymer
	Hydroxy Propyl Methyl Cellulose (HPMC)	Suspending agent, Emulsifying agent
	Triethyl citrate	Plasticizer
	Methanol	Solven

Table 2. List of equipments

S.N.	Materials	Category
	UV-vis spectroscopy	Shimadzu, Japan
	FTIR spectroscopy	Analytical Techno Pvt. Ltd (WQF 520)
	Digital electronic balance	Shimadzu, Japan
	Franz diffusion	Delhi Scientific, India
	Melting point apparatus	Macro Scientific Work, India
	Viscometer	Brookfield LVDV-II
	pH meter	Welltronics Pvt.. Ltd., Ahmedabad
	Magnetic stirrer	Remi lab instruments, India

Collection and authentication of selected plant

The fresh leaves of *Azadirachta indica* and *Ocimum sanctum* were collected from the UP east and authenticated from the botanist at BSI, Allahabad with reference no. 2023-24/529. These were cleaned, washed, and dried under shade. The plant materials were washed, shade dried and crushed into coarse powders.

Extraction of plant materials

The dried leaves of *Azadirachta indica*, and *Ocimum sanctum* were rendered into fine powder and extracted using distilled water and chloroform (1:1) solvent system through cold maceration process. The leaves of *Azadirachta indica*, and *Ocimum sanctum* were soaked in a beaker containing distilled water and chloroform (1:1) solvent system for 15 days with gradual stirrings, separately. Each beaker was mounted with aluminium foil. After the due time, each beaker's aluminium foil was removed and filtered using the cotton plug and finally with Whatman filter paper. The obtained slurry was made concentrated through evaporation using rotatory evaporator. Thus, the herbal extract was found in powder form and weight to calculate the % yield. All the extracts were kept in desiccator to keep the extract moisture free (Khan M.A. *et al.* 2020).

Preliminary phytochemical investigation

Preliminary phytochemical investigation of leaves extract of *Azadirachta indica* and *Ocimum sanctum* was carried out by qualitative chemical test and chromatographic technique (Devi and Kottai M.A., 2014; Alaekwe *et al.* 2015).

Alkaloids

Before filtration, each extract was individually treated in diluted HCl.

Mayer's Test: The filtrates were run on Mayer's reagent, potassium mercuric iodide. Alkaloids are present when a precipitate with yellow hue develops.

Wagner's Test: The filtrates were run on Mayer's reagent, potassium mercuric iodide. Alkaloids are present when a precipitate with yellow hue develops.

Hager's Test: The filtrates were treated with Hager's reagent. Yellow PPT shows the presence of alkaloids by forming.

Glycosides

Fehling's test: Fehling diluted with distilled water then heated his solutions A and B for one minute. Eight drops of plant extract were added to this crystal-clear solution. It then was combined with one millilititer of Fehling's solution and heated in a water bath for five minutes. Brick-red precipitation shows the presence of glycosides.

Saponins

Foam test: A consistent, long-lasting froth was achieved by rapidly shaking 10ml of distilled water with around 2g of the plant extract. There are saponins present when froth appears.

Tannins

Ferric chloride test: Twenty milliliters of water were used to boil 0.5 grams of the dried powdered material in a test tube, and then the mixture was filtered. Following the addition of a few drops of 0.1% FeCl3, the coloration was examined for blue-black or brownish green-black.

Lead acetate test: Two milliliters of plant extract and two milliliters of distilled water were combined. The liquid was well shaken after 0.01g of lead acetate was added. When precipitate and white turbidity form, tannins are present.

Flavonoids

NaOH test: After treating a little amount of extract with aqueous NaOH and HCl, the formation of a yellow-orange tint was observed.

H_2SO_4 test: A fraction of the extract was treated with Conc.H2SO4, and the emergence of an orange tint was observed.

Terpenoids

Following the addition of 2.0 ml of chloroform and 5 ml of the aqueous plant extract, the mixture was heated with 3 ml of concentrated H2SO4 and evaporated on the water route. When the terpenoids formed, they took on a gray color.

Fehling's test: It is used to identify sugars that are declining. 34.66 grams of copper sulfate should be dissolved in 500 milliliters of distilled water (solution A). 50 milliliters of distilled water should be used to dissolve 50 grams of sodium hydroxide and 17.3 grams of potassium sodium tartrate (Solution B). Mix two solutions in an equal volume before using. One minute should be spent boiling Fehling's A and B solutions in a 1 mL combination. Equal parts of the test solution should be added. For five to ten minutes, heat in a saucepan of boiling water. The color was originally yellow, and later brick red.

Steroids

Two milliliters of chloroform and concentrated H_2SO_4 were mixed with five milliliters of aqueous plant crude extract. The presence of steroids was shown by the redness that appeared in the bottom layer of chloroform.

Tests for reducing sugar & carbohydrate

Molisch's test
To 2-3 ml of extract of individual solvents, add a few drops of α-naphthol solution in alcohol, stir, and then add concentrate H_2SO_4 from the edges of the test tube. Two liquids meet to form a violet ring.

Chromatographical analysis

TLC analysis
The plant extracts (after dissolving in respective solvents) were placed to the precoated TLC plate in the form of dots using a fine capillary. The top of the plate had identification markings. Chromatography tests were performed in rectangular glass vessels. A smooth sheet of filter paper was inserted in the TLC chamber and left in the developing solvent to prevent insufficient chamber saturation and the unwanted edge effect. Anisaldehyde-sulphuric acid was sprayed on the plate, and then it was heated at 115 degrees Celsius for 5 minutes. The solvent system utilised was chloroform: ethyl acetate: acetone (7:1.5:1.5). Plates were developed, allowed to air dry, and then analysed for spot count, colour, and Rf values. Agents used for spraying anisaldehyde and sulfuric acid (Kumar S. *et al.* 2013).

$$Rf = \frac{\text{Distance traveled by the compound}}{\text{Distance traveled by the solvent front}}$$

HPTLC Analysis
The stationary Phase is typically a thin layer of silica gel or other adsorbents. The choice of stationary phase depends on the nature of the sample components (polar or non-polar). The mobile phase can be a mixture of solvents, depending on the solubility of the analytes. Common mobile phase can be a mixture of polar and non-polar solvents, which allow for optimal separation of components.

Sample preparation
Prepare the sample by dissolving the analyte in a suitable solvent. Filtration might be necessary to remove any particular matter. The sample is applied to the TLC plate in small volumes using a micropipette or a syringe. Sample application should be uniform and concentrated in one area.

Chromatographic Separation
The plate is placed in a developing chamber, where the mobile phase will move upward due to capillary action. Components of the sample will travel at different rates based on their interaction with the stationary phase, leading to separation. After development, the plate is dried and observed under UV light or through staining techniques for colorimetric analysis. Densitometric scanning (measurement of intensity of bands) will also be performed to quantity the separated components.

Preformulation studies

Compatibility studies of different plant extracts and excipients
To check for any changes in the herbal extract's chemical composition following its combination with the excipients/polymers. *Azadirachta indica* and *Ocimum sanctum* leaves extract (aqueous & chloroform) with potassium bromide was applied and pressed into the shape of a disc. The disc was examined using Shimadzu FTIR spectroscopy (4000-400cm-1).

Preparation of standard calibration curve of herbal extracts (λmax)
Standard stock solution was prepared by dissolving 10mg of *Azadirachta indica* and *Ocimum sanctum* leaves extract (aqueous & chloroform, separately) with 10ml of methanol to give a 1000μg/ml concentration. To develop stock II, which has a concentration of 100μg/ml, take 1ml of this stock solution and diluted it with methanol (solvent) up to 10ml. A 10ml volumetric flask was filled with 1ml of the stock solution (100μg/ml), and the line was then filled with methanol to a volume equal to 10μg/ml. The sample was then scanned with a UV-Visible spectrophotometer in the 200-400nm wavelength range using methanol as a blank. Further dilutions of 2μg/ml, 4μg/ml, 6μg/ml, 8μg/ml, 10μg/ml, and 12μg/ml were made from the stock solution (100μg/ml). The absorbance of the dilutions was measured at absorption maxima. The calibration curve was then constructed (Suksaeree J. *et al.* 2018).

Preparation of film-forming gel
Using the dispersion process, the Eudragit RS PO and Hydroxy propyl methyl cellulose polymer solution were created in methanol. Twenty milliliters of methanol containing triethyl citrate were used to disseminate Eudragit RS PO. Separately, hydroxy propyl methyl cellulose was dissolved in 15 milliliters of aqueous methanol. To get clear solutions, both solutions were left to swell for a whole day. The polymeric solutions were mixed correctly with continuous stirring at 50rpm for 30min. In a 1:1 ratio, 10 mg of the precisely weighed herbal extracts were dissolved in 15 ml of methanol. For 30 minutes, the drug solution and polymeric dispersion were thoroughly combined while being constantly stirred at 50 rpm.

Table 3. List of composition used in the formulation of film-forming gel

Ingredients	F1	F2	F3	F4	F5	F6
Leaf extract of *Azadirachta indica*	1%	1%	1%	1%	1%	1%
Leaf extract of *Ocimum sanctum*	1%	1%	1%	1%	1%	1%
Eudragit RS PO (w/v)	2	4	6	8	10	12
HPMC (w/v)	12	10	8	6	4	2

Triethyl citrate (w/w)	0.5	1.0	1.5	0.5	1.0	1.5
Ethanol: Water (v/v)	70:30	70:30	70:30	70:30	70:30	70:30

Evaluation parameters of film-forming gel

Physical appearance

The physical appearance was determined for the formulated film forming gel of different herbal extracts.

pH estimation

The pH was estimated for the formulated film forming gel utilized different herbal extracts using digital pH meter.

Drug content

The concentration of the drug was determined using a suitable analytical method after a precisely weighed piece of the film forming gel was dissolved in a suitable solvent in which the drug is soluble.

Spreadability

The ability to spread well is one of the requirements for a gel to meet the ideal standards. It is a word used to describe the area across which a gel spreads easily when applied to skin or another affected area. The spreadability value of a formulation affects its medicinal effectiveness as well. The spreading diameter of the gel (1g) between two horizontal plates of 20cm×20cm was measured to test the gel's ability to spread after one minute. To test spreadability, a standard weight of 125g was added to the upper plate. The spread circle's diameter was measured in centimetres, and the result is an average of three calculations (Gupta R and Gupta GD, 2017).

Drying time (in-vivo)

The mixture was applied to a volunteer's inner forearm sides in order to measure drying time. A glass slide was positioned on the film without any pressure after two minutes. After removal, the film was deemed dry if there were no liquid remnants visible on the glass slide. The experiment was repeated until the film was determined to be entirely dry if there were still liquid remnants visible on the glass slide (Sharma N. *et al.* 2011).

Film formation

A Petri dish was used to create the films. With or without the film-forming polymer precipitating, the film-formation process was assessed and scored as complete and uniform, incomplete, or non-uniform. The film's aesthetic qualities are described as follows: peelable or non-peelable, sticky, or dry, and transparent or opaque (Schroeder I. Z. *et al.* 2007).

Film flexibility

Stretching the skin in two or three directions allowed for the evaluation of film flexibility based on cracking and skin fixation. If there is no cracking or skin fixation, the film is considered flexible; if both are present, it is considered non-flexible (Shinde A.J. *et al.* 2008).

Film thickness

A glass substrate was coated with 1ml of each formulation's film forming solution, which was then allowed to evaporate for 15 minutes in order to produce a film. A micrometre screw gauge (Mitutoyo, Kanagawa, Japan) was used to measure the thickness of the produced films, and the result was the mean of three separate portions (Shinde A.J. *et al.* 2008).

Weight variation

The 10 randomly selected film weighed individually and average weight was recorded.

Folding endurance

A little strip of film (2cm×2cm) was put on a plastic sheet and folded repeatedly until it shattered to test the folding durability of films. It refers the no. of times that film could be folded (same spot) without breaking (Ammar H.O. *et al.* 2013).

***In-vitro* release study**

The diffusion investigations of the generated film forming gels were conducted in a Franz diffusion cell. The cell consisted of two chambers, the donor, and the receptor compartment between which a diffusion membrane (egg membrane) was mounted. The donor compartment, with inner diameter 24mm, was open i.e. exposed to the atmosphere at one end and the receptor compartment was such that it permitted sampling. The diffusion medium used was phosphate buffer solution pH 5.8 (PBS). 1ml of the drug containing film forming gel was placed in the donor compartment over the drug release membrane and was separated from the receptor compartment by the egg membrane. The egg membrane was previously soaked for 24hr. in PBS. The donor and receptor compartments were held together using a clamp. The position of the donor compartment was adjusted so that egg membrane just touches the diffusion medium. The whole assembly was fixed on a magnetic stirrer. The receptor compartment with 100mL of PBS was placed on thermostatically controlled magnetic stirrer. It was maintained at 37±0.5ºC and stirred constantly at 50 rpm. Samples of 1ml were collected at predetermined time intervals and analysed for drug content by UV Spectrophotometer at λ max against blank. The receptor phase was replenished with an equal volume of phosphate buffer at each time of sample withdrawal (Kulkarni S.V. *et al.* 2010).

RESULTS AND DISCUSSION

Percentage yield

The percentage yield of fresh leaves extract of *Azadirachta indica* was found as 48.32%. Moreover, fresh leaves extract of *Ocimum sanctum* showed the percentage yield of 43.56% when extracted using hydro-chloroform (1:1) solvent.

Organoleptic properties of herbal extracts

Table 4. Organoleptic properties of herbal extracts

Plant extract	Part used	Organoleptic characteristics		
		Appearance	Colour	Odor

Azadirachta indica	Leaves	Powder	Dark green	Characteristics
Ocimum sanctum	Leaves	Powder	Dark green	Characteristics

Preliminary phytochemical investigation

Table 5. Phytochemical investigation of herbal extracts

Phytochemical	**Leaves extract**	
	A. indica	*O. sanctum*
Alkaloids	++	++
Glycosides	+	+
Tannins	++	++
Saponins	++	++
Terpenoids	++	++
Steroids	+	++
Flavonoids	++	++
Phenols	+	++
Reducing sugars	_	_
Proteins	++	++
Carbohydrate	+	++

++: Abundance, +: Moderate; -: Absent

Chromatographical analysis

TLC analysis of herbal leaves extract

In leaves extract of *A. indica*, the Rf values were observed as 0.78, 0.74 and 0.71 in Chloroform: ethyl acetate: acetone (70:20:10), Chloroform: ethyl acetate: acetone (50:30:20), and Chloroform: ethyl acetate: acetone (70:15:15) fractions, respectively. However, *O. sanctum* leaves extract showed the Rf values as 0.81 and 0.79 in Chloroform: ethyl acetate: acetone (70:20:10), and Chloroform: ethyl acetate: acetone (50:30:20) fractions. Therefore, it can be said that among all 3 fractions, chloroform: ethyl acetate: acetone (70:20:10) was found more efficient in isolation of plant constituents.

Table 6. TLC analysis of leaves extract of *A. indica* and *O. sanctum*

Herbal extract	**Solvent system**	**R_f Value**
A. indica	Chloroform: ethyl acetate: acetone (70:20:10)	0.78
	Chloroform: ethyl acetate: acetone (50:30:20)	0.74
	Chloroform: ethyl acetate: acetone (70:15:15)	0.71
O. sanctum	Chloroform: ethyl acetate: acetone (70:20:10)	0.81
	Chloroform: ethyl acetate: acetone (50:30:20)	0.79
	Chloroform: ethyl acetate: acetone (70:15:15)	0.75

HPTLC Analysis

Table 7. HPTLC analysis of of *A. indica* and *O. sanctum*

Herbal extract	Solvent system	R_f Value	Expected compounds
A. indica	Chloroform: ethyl acetate: acetone (70:20:10)	0.78	Flavonoids and Tannins
	Chloroform: ethyl acetate: acetone (50:30:20)	0.74	
O. sanctum	Chloroform: ethyl acetate: acetone (70:20:10)	0.81	Flavonoids and Terpenoids
	Chloroform: ethyl acetate: acetone (50:30:20)	0.79	

Pre-formulation studies

Organoleptic properties

Along with the herbal extracts, other chemicals i.e., Eudragit RS PO, HPMC, and Triethyl citrate were observed for organoleptic properties. Eudragit RS PO was found as white powder and odourless. HPMC was found as off-white powder, and odourless. Triethyl citrate is a colourless liquid with fruity smell.

Table 8. Organoleptic properties

Ingredient	Organoleptic properties		
	P. state	Color	Odor
A. indica leaves extract	Powder	Dark green	Characteristics
O. sanctum leaves extract	Powder	Dark green	Characteristics
Eudragit RS PO	Powder	White	Amine-like
HPMC	Powder	Off-White	Odourless
Triethyl citrate	Liquid	Colourless	Fruity smell

Melting/Boiling point

The melting point was observed as 156°C and 226°C in Eudragit RS PO and HPMC, respectively. However, Triethyl citrate showed the boiling point as 294°C.

Table 9. Melting/Boiling point

Chemical	Melting/Boiling point	
	Sample	Reference
Eudragit RS PO	156°C	142-167°C
HPMC	226°C	225-230°C
Triethyl citrate	294°C (B. P.)	294°C (B. P.)

Estimation of solubility

Table 10. Solubility

Solvent	Solubility				
	A. indica leaves extract	*O. sanctum* leaves extract	Eudragit RS PO	HPMC	Triethyl citrate
Ethanol	Soluble	Soluble	Soluble	Soluble	Soluble
Methanol	Highly soluble	Highly soluble	Highly soluble	Highly soluble	Soluble
Phosphate buffer	Poor soluble	Poor soluble	Poor soluble	Poor soluble	Soluble
Tween 80	Readily soluble	Readily soluble	Readily soluble	Readily soluble	Readily soluble
Water	Poor soluble	Poor soluble	Insoluble	Soluble	Soluble

Std. Calibration curve of herbal extracts

The following table shows the conc. (µg/ml) of *A. indica* leaves extract and absorption (λmax 257 nm).

Table 11. Absorption of *A. indica* leaves extract

Conc. (µg/ml)	Absorption (λmax 257 nm)
2	0.17
4	0.33
6	0.51
8	0.67
10	0.83
12	0.94

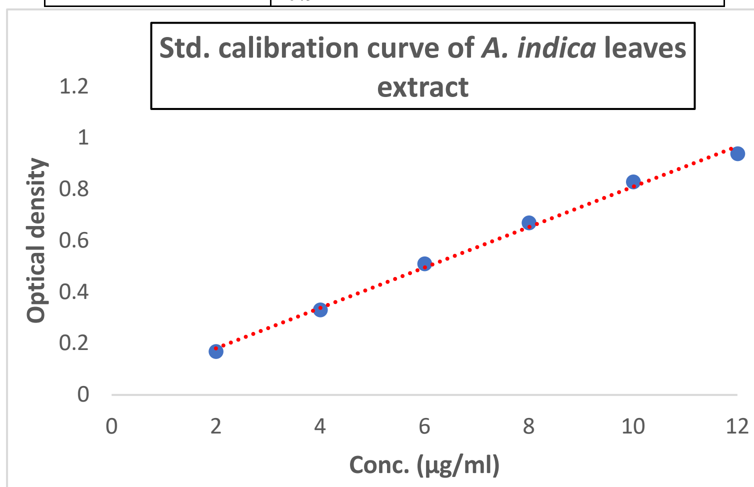

Fig 1. Std. Calibration Curve of *A. indica* leaves extract

The following table shows the conc. (µg/ml) of *O. sanctum* leaves extract and absorption (λmax 320 nm).

Table 12. Absorption of *O. sanctum* leaves extract

Conc. (µg/ml)	Absorption (λmax 320 nm)
2	0.14
4	0.29
6	0.43
8	0.64
10	0.82
12	0.95

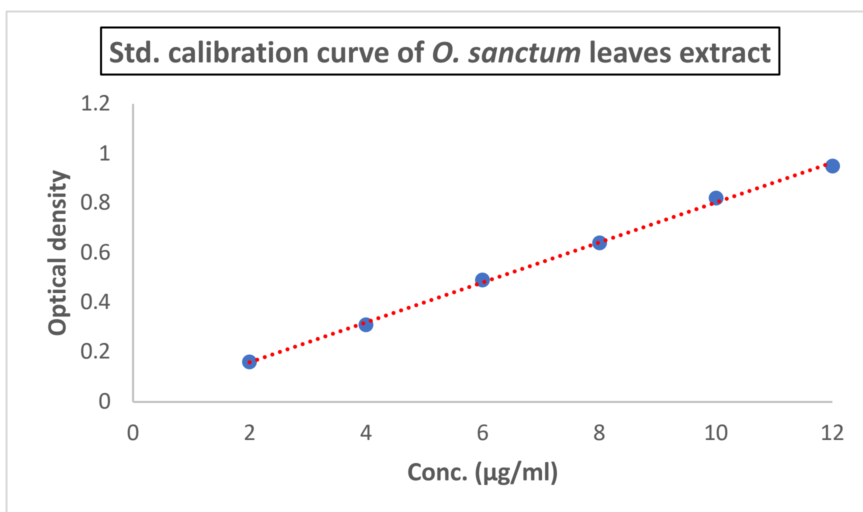

Fig 2. Std. Calibration Curve of *O. sanctum* leaves extract

Evaluation parameters of film-forming gel

Physical appearance (Film formation)

Table 13. Physical appearance of polyherbal film forming gel

Formulation	Physical appearance
F1	Non-transparent, Peelable
F2	Non-transparent, Peelable
F3	Non-transparent, Peelable
F4	Non-transparent, Peelable
F5	Non-transparent, Peelable
F6	Non-transparent, Peelable

pH estimation

Table 14. pH estimation of polyherbal film forming gel

Formulation	pH
F1	6.3±0.02
F2	6.8±0.05
F3	6.4±0.06
F4	6.6±0.03
F5	6.2±0.01
F6	6.5±0.04

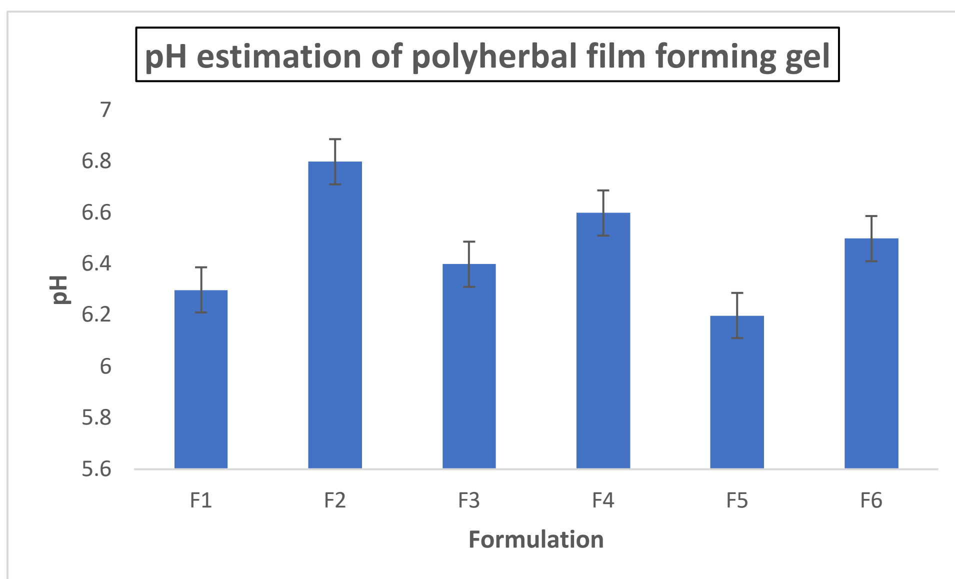

Fig 3. Graphical data of pH estimation of polyherbal film forming gel

Drug content

Table 15. Drug content of polyherbal film forming gel

Formulation	Drug content (%)
F1	91.45±0.32
F2	94.56±0.21
F3	96.41±0.34
F4	93.27±0.13
F5	98.12±0.14
F6	89.45±0.45

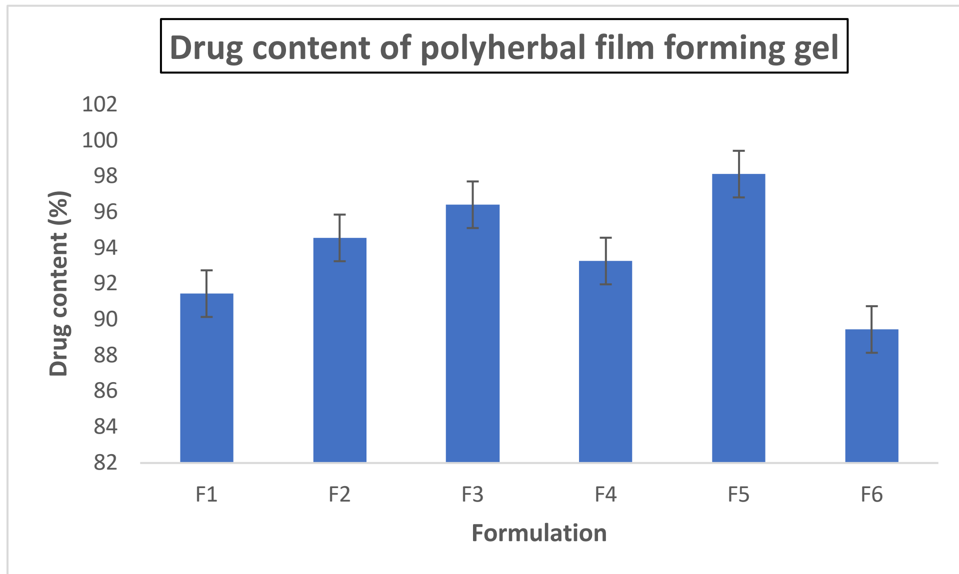

Fig 4. Graphical data of drug content of polyherbal film forming gel

Spreadability

Table 16. Spreadability of polyherbal film forming gel

Formulation	**Spreadability (g.cm/c)**
F1	3.25±0.45
F2	4.36±0.24
F3	4.67±0.20
F4	5.40±0.56
F5	6.17±0.23
F6	4.56±0.14

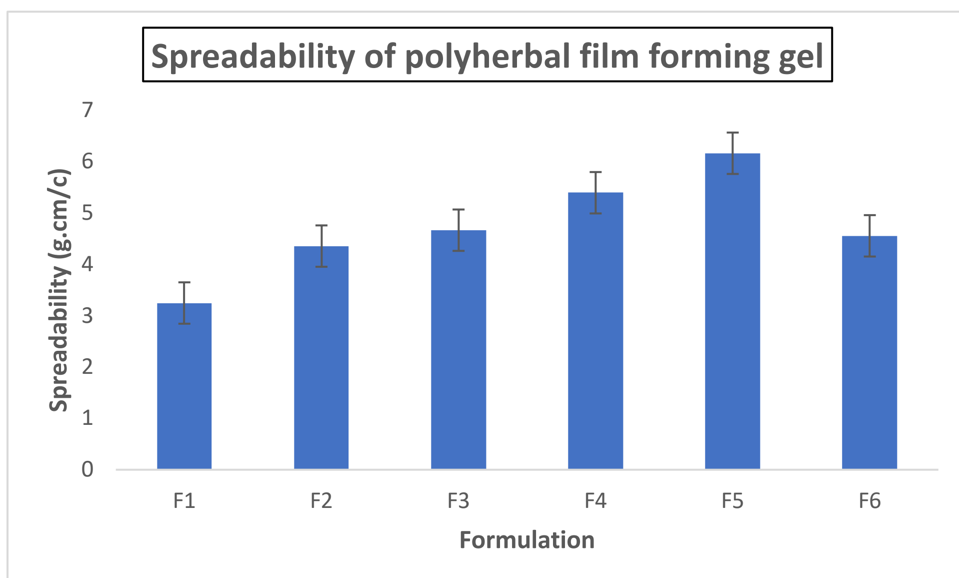

Fig 5. Graphical data of spreadability of polyherbal film forming gel

Drying time

Table 17. Drying time of polyherbal film forming gel

Formulation	Drying time (minutes)
F1	5
F2	6
F3	4
F4	5
F5	3
F6	6

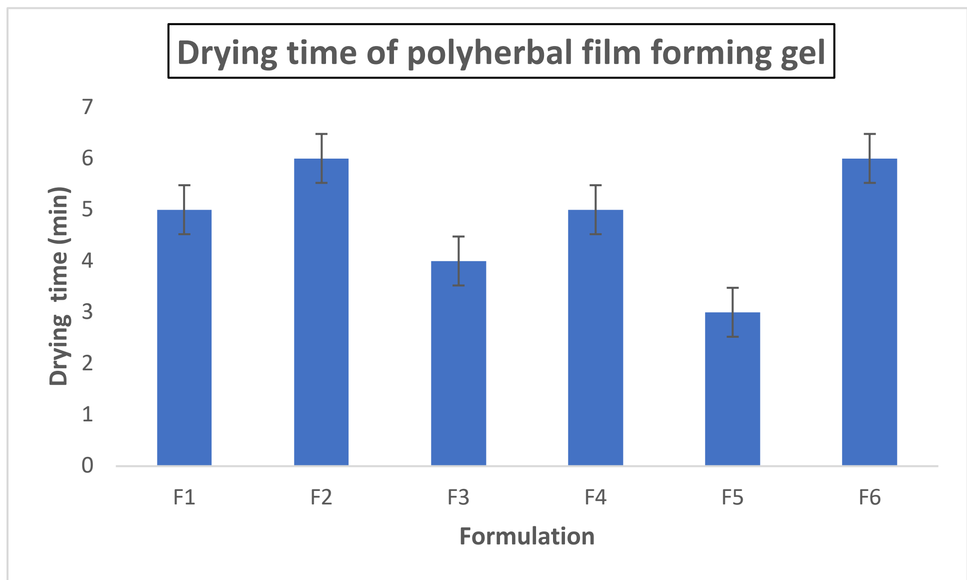

Fig 6. Graphical data of drying time of polyherbal film forming gel

Film flexibility

Table 18. Film flexibility of polyherbal film forming gel

Formulation	Film flexibility
F1	Non-flexible
F2	Non-flexible
F3	Flexible
F4	Non-flexible
F5	Flexible
F6	Non-flexible

Film thickness

Table 19. Film thickness of polyherbal film forming gel

Formulation	Film thickness
F1	0.14± 0.56
F2	0.16± 0.34
F3	0.17± 0.43
F4	0.19± 0.35
F5	0.13± 0.42
F6	0.15± 0.29

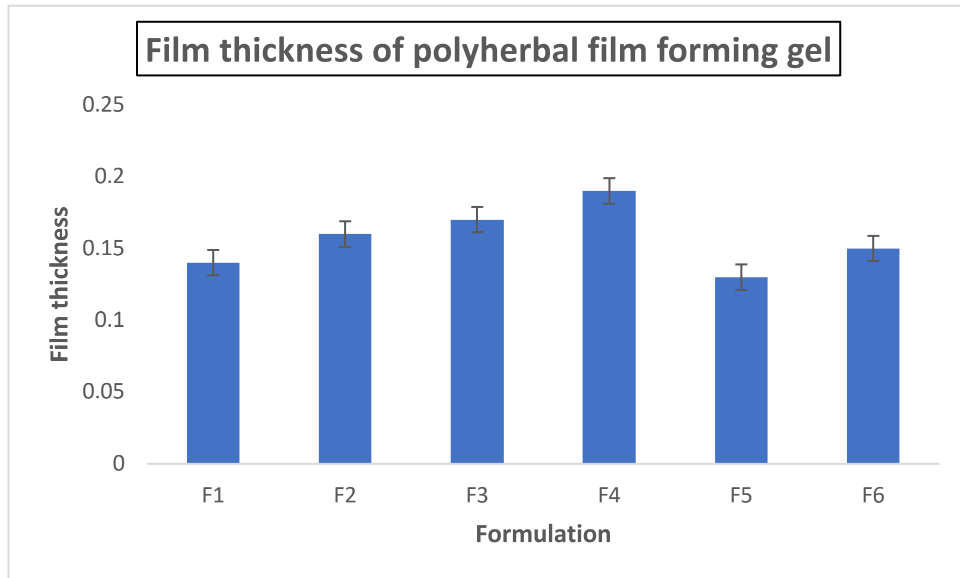

Fig 7. Graphical data of film thickness of polyherbal film forming gel

Weight variation

Table 20. Weight variation of polyherbal film forming gel

Formulation	Weight variation
F1	0.17± 0.07
F2	0.14± 0.05
F3	0.21± 0.02
F4	0.15± 0.06
F5	0.14± 0.03
F6	0.19± 0.04

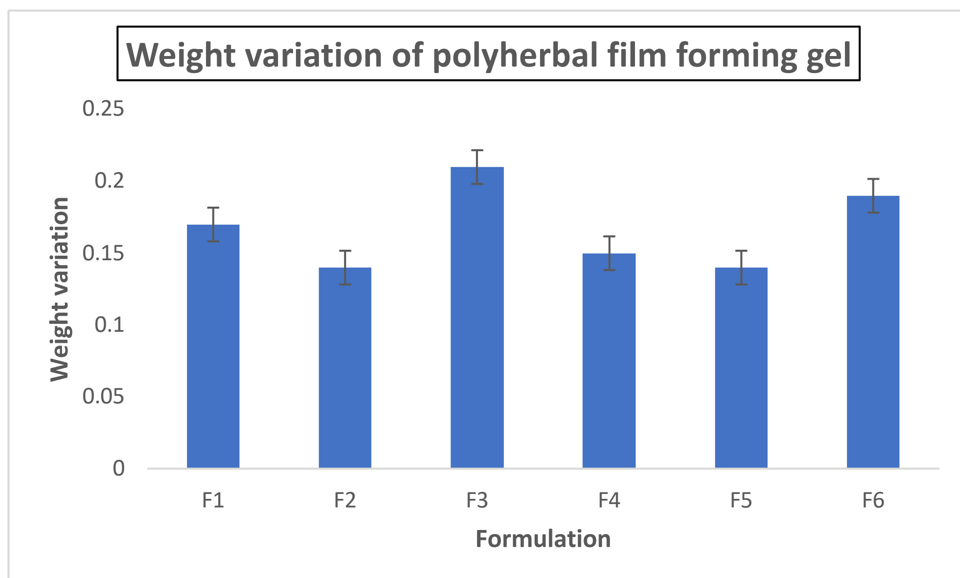

Fig 8. Graphical data of weight variation of polyherbal film forming gel

Folding endurance

Table 21. Folding endurance of polyherbal film forming gel

Formulation	**Folding endurance**
F1	94
F2	108
F3	89
F4	83
F5	112
F6	103

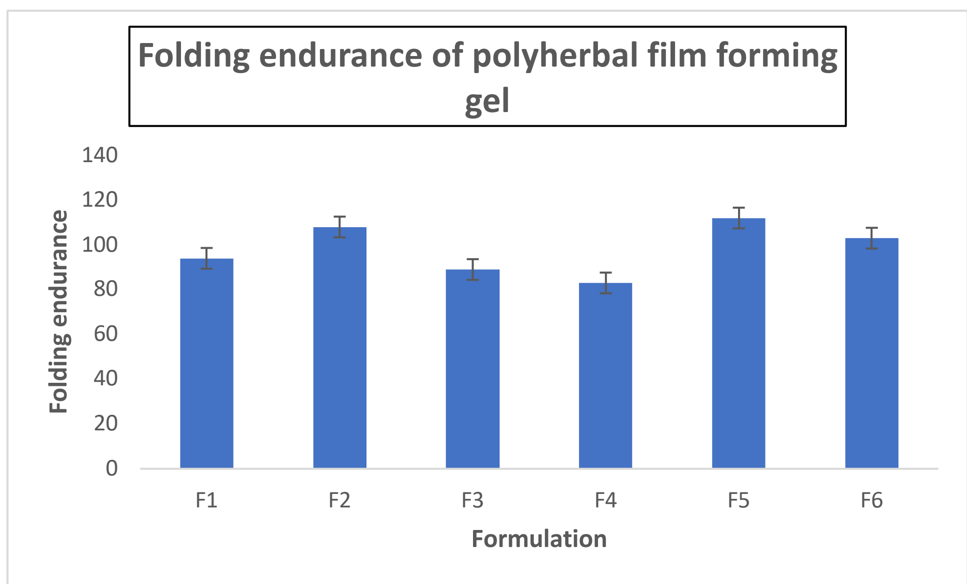

Fig 9. Graphical data of folding endurance of polyherbal film forming gel

***In-vitro* release**

Table 22. *In-vitro* release of polyherbal film forming gel

Time (hr)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
0.5	30.26	32.45	39.20	36.74	29.24	27.5
1	39.43	36.19	42.56	44.15	37.56	36.78
2	45.62	42.45	49.17	47.56	41.23	39.16
3	49.45	47.26	54.67	49.22	42.51	41.30
4	53.14	49.56	57.42	52.49	47.11	43.56
5	58.45	53.19	63.26	57.45	56.40	48.29
6	61.13	61.25	69.45	67.32	61.56	59.29
12	69.45	72.40	74.67	76.45	79.15	72.56
18	74.23	78.19	79.58	82.45	87.14	84.20
24	84.56	87.34	89.34	91.85	93.21	92.34

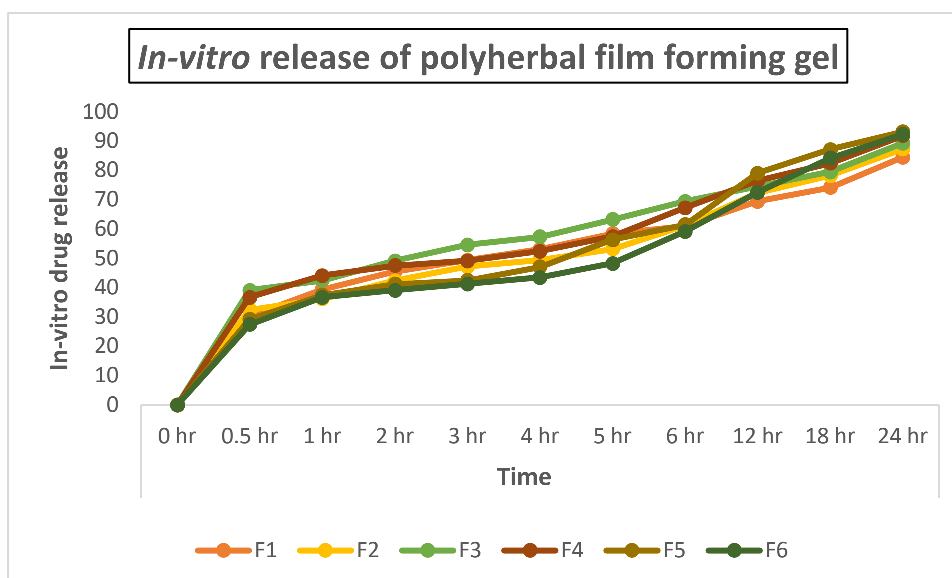

Fig 10. Graphical data of *in-vitro* release of polyherbal film forming gel

Nevertheless, a hydrophilic polymer matrix was created by the successful encapsulation of MF into NE. Furthermore, NE-loaded films could have become more hydrophilic when 12 weight percent of a hydrophilic surfactant was added, which would have impacted their ability to absorb water. As seen in Figure 13, the drug loading efficiency of NE-loaded films was higher (94.1±6.53) than that of the physical mixture film (72.8±6.11). It appears that MF was able to be encapsulated inside NE and successfully incorporate the medication into films due to the existence of nanosized droplets. NE tends to offer good stability due to their nanoscale droplet size, which drastically reduces the probability of droplets approaching and inhibits coalescence, which could lead to phase separation. The mometasone furoate nanoemulsion-based film's content uniformity was 95.14±8.9, whereas the control film's was 94.0±4.6, indicating that the drug was uniformly distributed throughout the films (Singh V K., et al. 2024).

Miconazole nitrate film-forming gel was made with hydroxypropyl cellulose and Eudragit RS PO. To achieve the best drug release and antifungal efficacy, the concentrations of both polymers were adjusted using a 32 complete factorial design. Thus, a methodical approach to formulation might lead to the achievement of desired goals. According to an antifungal investigation, the new film-forming gel is more effective than the commercial product since it may lower the fungus load. The study's film-forming dermal gel satisfies every requirement needed for topical application. The precision and placement of a dose will be enhanced by this innovative dosage form. The bioavaility of topical administration of Miconazole nitrate in gel form may be enhanced by the optimized formulation with superior bioadhesive properties, which might serve as an alternative to the topical formulations that are typically provided (Saudagar and Gangurde, 2017).

In order to reduce intraocular pressure, this effort aims to create a thermosensitive in situ gel of latanoprost as a topical ocular dose form. The ideal formula F3, which contains 18% PF127 and 1% HPMC E5%, has a sol-gel temperature of 34.3°C, a gel strength of 23.13g, and a mucoadhesion of 0.06 mJ. These characteristics lengthen the duration of contact between the medication and the tissues of the eyes, which may prevent the eye from draining too quickly and improve transcorneal penetration. This formula demonstrated a high flow of 11.4μg/cm2/hr, as the findings shown. When compared to a traditional eye drop (Ioprost), the formula showed the most notable and quick drop in IOP in a rabbit glaucoma model, with a 2.9-fold increase in AUC0-12. Furthermore, the results showed that the in situ gelling system loaded with latanoprost is more stable at various temperatures than the conventional eye drop. By reducing the frequency of administration, the in situ gelling device is expected to improve patient compliance. A non-invasive substitute for the traditional anti-glaucoma eye drop might be offered by this new Latanoprost thermosensitive in situ gel (Khattab A. et al., 2019).

According to a research, the formulation was created to achieve the following goals: maximal antifungal activity, drug content, film-forming properties, ideal drying duration, and desirable esthetic appearance. Drying time, viscosity, pH, spray angle, ex-vivo physical assessment, film mechanical characteristics, and in-vitro antifungal efficacy were all examined for the formulations. Ultimately, we draw the conclusion that the F5 formulation, which combines PVP K30 (10%w/w), Eudragit RS 100 (1%w/w), and propylene glycol (20%w/v of polymer weight) as a plasticizer in a solvent made up of a special ethanol:acetone (8:2) ratio, has the potential to be used as a film forming spray (FFS) for topical delivery of ketoconazole (Shaikh A G., et al., 2023).

In results, the formulated polyherbal extracts based film forming gel showed the optimized film formation & flexibility, pH, film thickness, spreadability, and drying time in F1-F6. The drug content and in-vitro drug release was also found excellent when determined for different time intervals i.e., 0, 0.5, 1, 2, 3, 4, 5, 6, 12, 18, 24 hours.

CONCLUSION

The most precise and efficient formulation was determined to be the F5. Desired characteristics such suitable viscosity, pH, spreadability, and drug release were shown in this formulation. This formulation produced a film that adhered well to the skin and released herbal extracts over time, which may increase patient compliance and treatment effectiveness. To improve this formulation for clinical use, further optimization and stability research are advised. Additionally, it demonstrates that the transdermal route of administration is acknowledged as one of the potential routes for the local and systemic delivery of drugs because it produces controlled release of the drug, which reduces systemic side effects, sometimes improves efficacy over other dosage forms, and increases patient compliance.
In conclusion, among all the films forming gel, F5 was selected as optimized formulation. Highest *in-vitro* release was found to be 93.21 % (F5) in 24 hours, which demonstrates a better sustained release formulation. It exhibited more significant characterization parameters and thus tested further for the anti-fungal activity on Wistar rats...

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