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FORMULATION AND EVALUATION OF HERBAL ANTIBACTERIAL GEL OF BETEL LEAF EXTRACT

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ABSTRACT

Piper betel, a plant famous for its therapeutic nature, is consumed in Asian countries like India, Nepal because of its characteristic taste, religious purpose. Betel leaf is a famous home solution for cerebral pain. Betel leaf juice is credited with diuretic properties. Betel leaves are valuable in aspiratory fondness in youth and mature age. Betel leaf is a superb family cure in the treatment of hack and sore throat, Applied locally, betel leaves are advantageous in the treatment of irritation, Betel leaves can be utilized to mend wounds. The juice of a couple of leaves ought to be separated and applied to the injury. Piper betel shows Antibacterial action on the skin, it reveals a prominent effect on bacterial disease, due to climate-changing skin pH varies from time to time, which provides a medium to grow bacteria which results in a bacterial diseases like eczema. Rashes. Nowadays there are so many types of topical drug formulations present in the market but the study aims to reboot the traditional system of medication because the organic molecules create dependence for our body & for this, our body easily creates tolerance for the particular drug. In our study, we used plant piper betel to determine its antibacterial properties. The activity involves, selection of plant, collection of leaves, Dethanolic extract, phytochemical & pharmacological study. The disc platetest method is used for the examination of antibacterial activity.

KEYWORDS:- Antibacterial activity, piper betel, uv spectroscopy, bacterial disease, herbal gel, pH determination, disc plate method.

INTRODUCTION

Topical drug therapy is generally utilized for the prominent effect in the area of their utilization by property of medication infiltration at the fundamental layers of skin or mucous layers. The fundamental compelling advantage of an effective conveyance framework is to sidestep the first-pass metabolism. To avoid the risk of drug metabolism, limitation of intravenous medication and of the different parameters of ingestion, similar to pH changes, presence of chemicals, gastric purging time are the beneficial advantage of topical drug delivery. Semi-solid formulations in the entirety of their distinction administer the framework for effective conveyance generally shower, cured powders, solutions, and even medicated adhesive drug therapies are being used. The skin drug conveyance framework is normally utilized where the other system of medication fails or it is primarily utilized in treatment in pain, contraception, and urinary impairment. In the course of the most recent decades, the treatment of ailment has been idealized by administrating medications to the human body by means of various courses specifically oral, sublingual, rectal, parental, skin, inward breath, and so forth. Skin drug conveyance can be characterized as the utilization of a medication containing definition to the skin to legitimately treat cutaneous issues (for example skin inflammation) or the cutaneous articulation of a disease (for example psoriasis) with the significance of limiting the pharmacological or other impacts of the medication to the outside of the skin or inside the skin. Skin exercises could conceivably require intra-cutaneous entrance. Topical medication conveyance frameworks contain an enormous decent variety of drug dose structures like semisolids, liquid formulations, spray, and medicated powders. The most generally utilized semisolid dosage form for skin drug preparations contain gels, creams.

The tropical drug formulations connote the use of medication onto the body utilizing ophthalmic, rectal, vaginal, and skin as the course of administration. Skin is one of the most effectively admittable organs on the human body for skin drug conveyance and assembles the central course for skin application. For the local preparation of effective ailments just as for restorative purposes, various definitions, altogether from solids to semisolids and liquid formulation are accessible to physicians, practitioners, and patients. Inside the classification of semisolid arrangements, transdermal gels offer incredible potential for application in the restorative and pharmaceutical industry. External utilization of gel at skin proposes certain obvious advantages like hasty arrival of medication straightforwardly to the site of activity, free of water solvency of medication when contrasted with creams and ointments.

Drug: Betel leaf

a. **Biological source:-** It is obtained from dried of leaves of Piper betel.

b. **Family:** Piperaceae,

c. **compound constituents:-** Plant contains a terpinene, P-cymene, carvacrol, chavicol and its subsidiaries, allyl catechol, eugenol, estragol, oxalic corrosive, malic corrosive, and amino acids. Leaves contain great measures of nutrients especially nicotinic corrosive, ascorbic corrosive, and carotin. They additionally contain huge measures of all fundamental amino acids aside from lycine, histidine, and arginine. Enormous groupings of asparagines are available while glycine and proline happen in great sum. The basic oil of leaves gives it the fragrant flavor. β-sitosterol is available in the root.

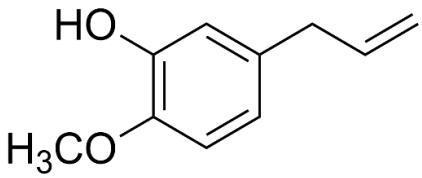

Fig. 10: Structure of chavibetol.

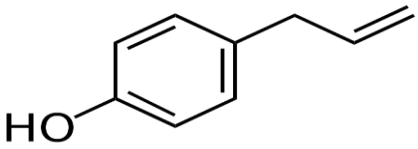

Fig. 11: Structure of chavicol.

d. Uses of betel leaf: Conventional employments of Betel leaves: The utilization of betel leaf can be followed as far back as 2,000 years. Betel leaves help to mend the accompanying ailments. For example,

1. **Headache:** Betel leaf is a famous home solution for cerebral pain. The betel leaf has pain-relieving and cooling properties. It tends to be applied with helpful outcomes over the agonizing territory to soothe exceptional cerebral pain.
2. **Scanty or obstructed urination:** Betel leaf juice is credited with diuretic properties. Its juice, blended in with weaken milk and improved marginally, helps in facilitating pee.
3. **Weakness of nerves:** Betel leaves assume an imperative function in the treatment of anxious agonies, apprehensive depletion, and debility. The juice of a couple of betel leaves, with a teaspoon of nectar, will fill in as a decent tonic. A teaspoon of this can be taken two times per day.
4. **Sore throat:** Betel leaf is a superb family cure in the treatment of hack and sore throat. Neighborhood utilization of the leaves is compelling in treating sore throat. The squashed organic product or berry ought to be blended in with nectar and taken to soothe bothering hack.

5. **Respiratory disorders:** Betel leaves are valuable in aspiratory fondness in youth and mature age. The leaves absorbed mustard oil and warmed, might be applied to the chest to soothe hack and trouble in relaxing.
6. **Constipation:** In the instance of obstruction in kids, a suppository made of the tail of betel leaf plunged in castor oil can be presented in the rectum. This in a flash diminishes blockage.
7. **Problem of breast milk secretion:** The use of leaves spread with oil is said to advance the emission of milk when applied to the bosoms during lactation.
8. **Inflammation:** Applied locally, betel leaves are advantageous in the treatment of irritation, for example, joint pain and orchitis that is the aggravation of the testicles.
9. **Wounds:** Betel leaves can be utilized to mend wounds. The juice of a couple of leaves ought to be separated and applied to the injury. At that point, a betel leaf ought to be folded around and bound. The injury will recuperate up with a solitary application inside 2 days.
10. **Boils:** Betel leaf is additionally a successful solution for bubbles. A leaf is delicately warmed till it gets mollified and is then covered with a layer of castor oil. The oiled leaf is spread over the exciting part. This leaf must be supplanted, like clockwork. After a couple of utilizations, the bubble will burst to deplete all the purulent issue. The application can be made around evening time and eliminated in the first part of the day.

Extraction of betel leaf

A. Assortment and Authentication of Piper betle leaves

The collected material was cleaned & driedunder shade (at ambient temperature) and then in oven at 20to40C. The dried leaves were weighed (100gm) & stored in desiccator.

B. Extraction of plant material

The extraction was done by Simple Maceration Process.The plant material (100gm) were mixed in double distilled water (1000ml) & 3% chloro form, placed for 7days under room temperature with occasional shaking. The mixture wasfiltered with muslin cloth, simple filter paper & then finally with Whatmann filter paper to obtain clear liquid extracts.

Phytochemical Screening and Preformulation study

A. Chemical test: Chemical test was performed by the ethyl alcohol drug extract of piper betel using standard norms to identify following constituents.

1. **Procedure for alkaloids:** 2ml of extract was taken & added 2ml of wagner's reagent gave brownish precipitate reveals the presence of alkaloids.
2. **Cardiac glycosides:** 2ml of extract was dissolved with 2ml of chloroform and concentrated sulphuric acid was cautionly added to form a layer. Deep reddish brown colour was found at the inter face of steroid ring shows the presence of cardiac glycosides.
3. **Flavonoids:** 2ml of drug extract was treated with 2 ml of 10%lead acetate. Yellowish green colour gaves the presence of flavonoids.
4. **Saponins:** 2ml of drug extract was dissolved with 2ml of Benedicts reagent. Blue black precipitate reveals the presence of saponins.
5. **Tannins:** 2ml of drug extract was treated with 0.1% of ferric chloride. Brownish green shows the presence of tannin chemical entity.
6. **Terpenoides:** (Salkowski test) 2ml of drug extract was measured & dissolved with 2ml of chloroform and concentrated sulphuric acid is cautionally added to form a layer. A reddish brown color shows the presence of terpenoids.
7. **Anthraquinones:** 1ml of extract was boiled with 10% HCL for few minutes in a water bath. It filtered and allowed to cool. Equal volume of CHCl3 added to the filtrate few drops of 10% Ammonia was added to the mixture and heat. Formation of rose pink color shows the presence of anthraquinones.

Table no. 1: Chemical test of herbal betel leaf.

S.no	Chemical test	Observation	Result
1.	Tannins	Brownish green Color	Positive
2.	Anthraquinones	Rose pink colour	Positive
3.	Flavanoides	Yellowish green colour	Positive
4.	Alkaloides	Brownish precipitate	Positive
5.	Terpenoids	Reddish brown colour	Positive
6.	Saponins	Blue black ppt	Positive
7.	Cardiac glycosides	Reddish brown colour	Positive

B. Solubility profile: 10 ml amount of Distilled water, ethanol, chloroform, propylene glycol was measured and subjected to determination solubility profile of betel leaf extract, followings are the observation

Table no. 2: Solubility profile of betel leaf extract.

S. no	Solvent	Solubility
1.	Distilled water	Soluble
2.	Ethanol	Soluble
3.	Chloroform	Soluble
4.	Propylene glycol	Soluble

C. Quantitative estimation

- Materials and methods:-

A) Advancement of adjustment bend selection of media

The selection of media was done onthebasis of drug solubility. Phosphatebuffer of pH 7.2 was selected for preparation of calibration curve.

B) Scanning for λmax

One hundred mg of crude extract was dissolved in little volume of phosphate buffer of pH 7.2 finally diluted to 100 ml in volumetric flask to get a concentration of 1000 µg/mL. This was treated as stock solution. Various aliquots of stock solution were to get different concentrations. Resultant solutions were scanned for λmax in the range of 200-400 nm using UV- spectrophotometer.

C) Preparation of calibration curve

Aliquots of the stock solution of PBL extract (1000µg/ml) pipetted out into series of 10 ml volumetricflasks & diluted wit phosphate buffer of pH 7.2 to get a final Concentration 20 to 100µg/mL. The absorbance of the resultant solutions was measured at 280nm. Freshly prepared solutions were made for the calibration curve on three consecutive days.

Table no. 3: UV Spectroscopy analysis.

S. no	Concentration µg/ml	Absorbance
1.	2	0.053
2.	4	0.098
3.	6	0.164
4.	8	0.221
5.	10	0.276

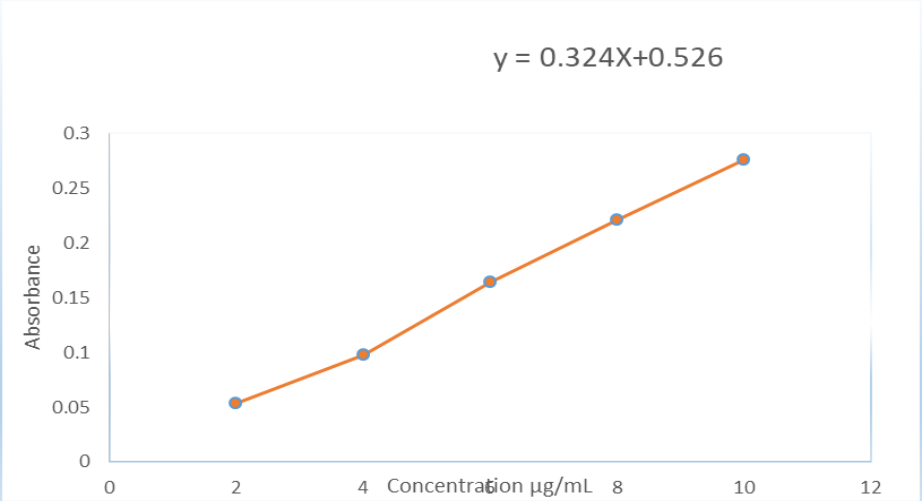

Fig. 12: Calibration curve of UV spectroscopy of betel leaf extrac

8. Preparation and evaluation of herbal antibacterial gel

A. **Preparation technique: -** triethanolamine was Dissolved in a little bit of water. Dissolved carboxy vinyl polymer in the blend, remaining measure of water was included into it .dissolvedthe additives in propylene glycol, the earlier blend was then added. when the gel was uniformed, perfume was included.

Formula

Table no. 4: Preparation of herbal antibacterial Betel leaf extract gel.

S.No	Ingredients	Quantity In Gm (F1)	Quantity 9 In Gm (F2)	Quantity In Gm (F3)
1.	Carboxyvinyl polymer	2.0	1.5	1.4
2.	Propylene glycol	9.0	9.5	9.6
3.	Triethanolamine	1.5	1.5	1.5
4.	Exract	5.0	5.0	5.0
5.	Water	82.5	82.5	82.5
6.	Perfume	q.s	q.s	q.s
7.	preservative	q.s	q.s	q.s

B. Characterization of herbal betel leaf extract gel

1. **Measurment of pH:-** The pH of created gel definitions was resolved to utilize advanced pH meter. 1 gm of the gel was disintegrated in 100 ml refined water and saved aside for two hours. The estimation of pH of every detailing was done in three-fold and normal qualities are determined. The pH estimations of all readied plans extended from 6-7 which are viewed as worthy to evade the danger of bothering upon application to the skin since grown-up skin pH is 5.5.

Formula: F1= 6.9+6.8+7.0 /3=6.9

F2=6.6+6.5+6.7/3=6.6

F3=6.4+6.5+6.6/3=6.5

Table no. 5: pH investigation.

Formulations	pH
F1	6.9
F2	6.6
F3	6.5

2. **Spreadability:-** Spreadability was dictated by the device which comprises a wooden square, which was given by a pulley toward one side. By this technique, spreadability was estimated on the premise of slip and drag attributes of gels. An overabundance of gel (around 2 gm) under investigation was set on this ground slide. The gel was then sandwiched between this slide and another glass slide having the element of the fixed ground slide and furnished with the snare. One kg weighted was put on the head of the two slides for 5 min. to remove air and to give a uniform film of the gel between the slides. An overabundance of the gel was rejected off from the edges. The top plate was then exposed to a pull of 80 gm. With the assistance of string joined to the snare and the time (in sec.) required by the top slide to cover a separation of 7.5 cm be noted. A shorter stretch demonstrates better spreadability.

The equation used to calculate Spreadability:

$S=M \times L/T$

Where S= Spreadability

M= Weight (in the slide)

L= Length moved by the glass slide

Table no. 6: Spreadability of betel leaf extract gel.

Formulation	Spreadability (gm/sec)
F1	9
F2	8
F3	6.8
Patanjali AloeVera Gel(standard)	12

3. **Extrudability:** The gel details were filled in standard topped folding aluminum tubes and fixed by pleating as far as possible. Loads of the cylinders were recorded. The cylinders

were put between two glass slides and were braced. 500 gm was set over the slides and afterward, the top was taken out. The measure of the expelled gel was gathered and gauged. The level of the expelled gel was determined (>90% extrudability: magnificent, >80% extrudability: great, >70% extrudability: reasonable).

Table no. 7: Extrudability of herbal betel leaf extract gel.

Batches	Weight of formulation (in gm)	Weight of gram extruded (in gm)	Extradibility amount (in gm)
F1	50	45.3	90.6
F2	50	44.1	88.2
F3	50	43.8	87.6

4. **Rheological study:** 10gm measure of the gel was taken and the consistency of the formed herbal betel leaf gel was dictated by utilizing Brookfield viscometer (Brookfield viscometer RVT) with spindle No. 7.

Table no. 8: Viscosity of herbal betel leaf extract gel.

Formulation	Viscosity (Cps)
F1	4237±0. 11
F2	4124±0. 43
F3	4014±0. 21

5. **In-vitro antimicrobial screening**

In vitro antimicrobial movement of the ethanol concentrates of betel plant was screened against two bacterial strains. Plate dispersion strategy the antimicrobial action of ethanol concentrate of betel plant was screened utilizing the circle dissemination method. The agar plates were set up by pouring 15 ml of liquid supplement agar media into sterile Petri plates. The plates were permitted to cement and 0.1% inoculum suspension was cleaned consistently with sterile cotton and was permitted to represent 15 minutes. The various weakenings of concentrates (0, 20, 40, 60, and 80%) from starting centralization of 1 mg/ml were stacked on 6 mm autoclaved channel paper plates. The stacked circle was put on the outside of the medium and the compound was permitted to diffuse for 5 minutes and the plates were brooded at 37°C for 24 hrs. Toward the finish of hatching, restraint zones conformed to the plate were estimated with a ruler in millimeter.

Table no. 9: Antibacterial activity of herbal betel leaf extract gel.

Bacterial strain	Zone of inhibition (in mm) F1	F2	Standard{Ciprofloxacin)	F3
Pseudomonas aeruginosa	14	16	13.5	18
S.auerus	12	13.5	11.6	15

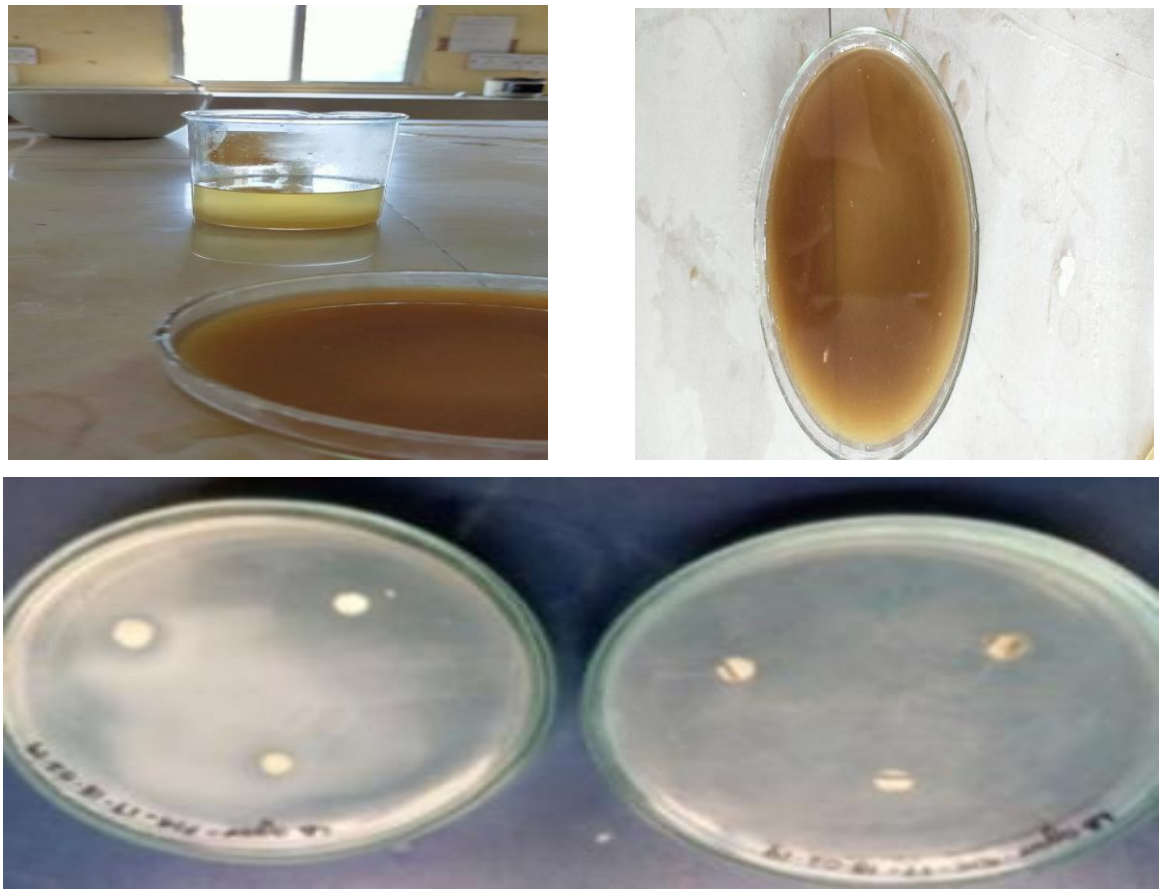

Fig. 13: Preparation of culture medium.

6. **Stability study of betel leaf gel:** stability investigations of gel were as per ICH guidelines. All the chosen arrangements were exposed to a dependability testing for one month according to ICH standard at a temperature of 40 ±2 °C. All the chose preparations were analyzed for the change in appearance, pH (ICH rules eighth, 2003).

Table no. 10: Stability study of herbal antibacterial gel.

Formulation	Days	pH	Homogenecity
F1	0	6.7	Excellent
	15	6.7	Excellent
	30	6.6	Good
F2	0	6.8	Excellent
	15	6.7	Excellent
	30	6.8	Excellent
F3	0	6.8	Excellent
	15	6.7	Excellent
	30	6.6	Excellent

RESULT

All procedures of standardization of were performed and it is listed below:

Table no. 1: Result obtained from chemical test of herbal betel leaf.

S.no	Chemical test	Observation	Result
1.	Tannins	Brownish green Color	Positive
2.	Anthraquinones	Rose pink colour	Positive
3.	Flavanoides	Yellowish green colour	Positive
4.	Alkaloides	Brownish precipitate	Positive
5.	Terpenoids	Reddish brown colour	Positive
6.	Saponins	Blue black ppt	Positive
7.	Cardiac glycosides	Reddish brown colour	Positive

Table no. 2: Result obtained from solubility profile of betel leaf extract.

S. no	Solvent	Solubility
1.	Distilled water	Soluble
2.	Ethanol	Soluble
3.	Chloroform	Soluble
4.	Propylene glycol	Soluble

Table no. 3: Result obtained from UV Spectroscopy analysis.

S. no	Concentration µg/ml	Absorbance
1.	2	0.053
2.	4	0.098
3.	6	0.164
4.	8	0.221
5.	10	0.276

Table no. 4: Result obtained from pH investigation.

Formulations	pH
F1	6.9
F2	6.6
F3	6.5

Table no. 5: Result obtained from Spreadability of betel leaf extract gel.

Formulation	Spreadability (gm/sec)
F1	9
F2	8
F3	6.8
Patanjali AloeVera Gel(standard)	12

Table no. 6: Result obtained from extrudability of herbal betel leaf extract gel.

Batches	Weight of formulation (in gm)	Weight of gram extruded (in gm)	Extradibility amount (in gm)
F1	50	45.3	90.6
F2	50	44.1	88.2
F3	50	43.8	87.6

Table no. 7: Result obtained from viscosity of herbal betel leaf extract gel.

Formulation	Viscosity (Cps)
F1	4237±0. 11
F2	4124±0. 43
F3	4014±0. 21

Table no. 8: Result obtained from antibacterial activity of herbal betel leaf extract Gel.

Bacterial strain	zone of inhibition (in mm) F1	F2	F3	Standard{Ciprofloxacin)
Pseudomonas aeruginosa	14	16	13.5	18
S. auerus	12	13.5	11.6	15

Table no. 9: Result obtained from stability study of herbal antibacterial gel.

Formulation	Days	pH	Homogenecity
F1	0	6.7	Excellent
	15	6.7	Excellent
	30	6.6	Good
F2	0	6.8	Excellent
	15	6.7	Excellent
	30	6.8	Excellent
F3	0	6.8	Excellent
	15	6.7	Excellent
	30	6.6	Excellent

DISCUSSION

The drug isolation, preparation, characterization was performed as per the standard procedure.

The standard prescribed in official books for determination of solubility, extrudability, spreadability, pH, determination of lambda max, the antibacterial test procedure was adopted for better study of betel leaf preparation.

The physical appearance of Gel was found to be uniform with a stable consistency.

Different chemical tests of Betel leaf were performed and all results of the test were found to be positive, which clearly gives the appropriate indication of Betel leaf.

Distilled water, propylene glycol, chloroform, ethanol, were selected as solvents for performing solubility. solubility of Betel leaf was found to be soluble in all above solvents.

The Betel leaf Extract was soluble in Distilled water, chloroform, ethanol, propylene, glycol. Phosphate buffer of Ph 7.2. The λmax of drug in phosphate buffer pH 7.2 was determined using UV spectrophotometer.

The λmax was determined by scanning 100 µg/mL solution of drug in the test medium in the range of 200-400 nm.

The λmax was found to be 280 nm and the absorbance was found to be in 0.053, 0.098, 0.164, 0.22, 0.276.

The extract was found & obey Beer-Lambert's law in the concentration range of 2-10µg/mL with regression coefficient (r^2) values 0.9998. The regression were calculated as y = 0. 324. X+0. 525 for phosphate buffer of pH 7.2.

The pH of the formulation F1, F2, F3 was found 6.9, 6.6, 6.5.it is near to be the skin pH which avoids the risk of irritation.

The spreadability of the F1, F2, F3 & standard was found to be 9,8,6.8 & 12.It is satisfactory and near to marketed gel preparation.

The extrudability of formulation F1, F2, and F3 was found to be 90.6%, 88.2%, 87.6%. The prepared gel of betel leaf returns a suitable amount of Extrudability.

Rheology is an important physical property of topical formulations, which affects the rate of drug release. The viscosity of the herbal antibacterial gel of betel leaf was determined by Brookfield viscometer. The viscosity of the F1, F2, F3 was found to be 4237±0.11, 4124±0.43, 4014±0.21 (in Cps) & it reveals that it possesses good homogeneity.

The gel showing well accepted physiochemical properties were finally selected for antibacterial activity. The zone of inhibition of betel leaf gel was compared with standard ketoconazole was found to be as In F1 it was found 14&12mm at the selected bacterial strain. In F2 it was found 16&13.5mm at the selected bacterial strain. In F3 it was found 13.5 & 11.6mm at the selected bacterial strain. In standard (Ciprofloxacin) it was found 18&15mm at selected bacterial strain respectively.

This study shows that the antibacterial activity of herbal betel leaf gel significant and it reveals that in the future there is a lots of scope of herbal in pharmaceutics, which gives low side effects as compared to the allopathic formulation.

Stability study was performed, the gel reveals that the prepared gel show good compatibility with excipients and prepared formulation can withstand in all seasons of year.

CONCLUSION

All parameters of an ideal gel was performed as standard norms, from the research study we envisaged that the prepared formulation fulfilled all suitable criteria of elegant & ideal gel with prominent therapeutic activity.it is helpful for the future aspect of the scope of herbal

medicine in the pharmaceutical industry. Herbal drug formulation gives low side effects as compared to Allopathic drug dosage formulation. The herbal topical formulation may be an alternative therapy for skin diseases. Our research study shows that herbal medicine is convenient for both the prescriber and the patient.

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