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Research Paper

Design of Derma Sticks of Tulasi for the Treatment of Skin Disorders

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ABSTRACT: *Vaginitis is described medically as an irritation and/or inflammation of the vagina. It is a very common disease affecting millions of women each year. The three most common vaginal infections reported each year are bacterial vaginosis (30-40%), candidiasis due to yeast infection (20-25%) and trichomoniasis caused by protozoal infection (15-20%). Vaginal infections can produce a variety of symptoms, such as abnormal or increased discharge, itching, fishy odor, irritation, painful urination or vaginal bleeding .Though the infections are not serious in nature, they can become chronic and the eradication of such infections is often difficult. If left untreated, bacterial vaginosis may result in increased risk of pelvic inflammatory disease (PID), infertility, pre-term birth, premature rupture of membranes, low birth weight, intra-amniotic infections, endometritis, cervical intra-epithelial neoplasia (CIN), post-gynecological surgery infections and increased risk of sexually transmitted diseases . Vaginitis is identified by checking vaginal fluid appearance, vaginal pH and presence of volatile amines (the odor causing gas) and microscopic detection of clue cells . Current medical therapy for vaginitis includes the use of systemic or topical antibiotic and antifungal preparations. Vaginitis being a disorder of multifactorial etiology a single-line therapy is often inadequate and recurrence is a common complication. Though these medications may temporarily reduce infection, they often disrupt the balance of good bacteria and frequently lead to recurrent infection. Studies shows that vulvovaginal candiasis (VVC) affects three-quarters of women during their lifetimes and use of antibiotics is an acknowledged trigger for VVC, which adversely affects women's physical and emotional health .*

Therefore as an alternative to these medications herbal therapy is gaining popularity of women on account of its reduced side effects and restoration of the normal vaginal flora .Gynecological skin disorders referring to inflammatory and infectious conditions affecting the vaginal mucosa and vulvitis often accompanies vaginal pain, itching and burning sensation. The topical drug delivery systems available for the treatment have several disadvantages like greasiness, inconvenient to store and requires applicator or use of fingertip, which may lead to contamination. Therefore, it was found essential to find an alternative to counter all the above disadvantages effectively and hence in the present work, formulation and development of medicated sticks has been planned with the herbal drug Tulasi which is very well known for the anti bacterial and anti fungal activity. The preparation and characterization of medicated sticks was carried out in four phases. Phase I studies includes preparation of medicated derma sticks using the ointment bases with varied concentrations of waxes. Phase II studies involves characterization of prepared medicated derma sticks like weight, thickness and length. Phase III studies involves stability studies of prepared formulations. Phase IV Studies involves anti microbial studies by zone inhibition method...Phase V: Primary skin irritation studies carried out on rabbits and guinea pigs and in healthy human volunteers. Showed no sensitization and edema on skin after 72 hrs of application.. The results of present study revealed that the prepared medicated sticks of Tulasi are convenient, equally effective, without any contamination chances on application and free from skin irritation.

Keywords: *Tulasi , medicated derma sticks*

I. INTRODUCTION

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Gynecological skin infections are very common in most of the woman population especially in rural areas due to unhygienic maintenance. Many patients express difficulty in application of ointments, creams, gels etc. results in non- compliance and ineffective therapy. Recent advance in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for application and to achieve better patient compliance. One such approach is medicated sticks[1-2]. An advantage of this drug delivery system includes patient compliance; convenience and comfort ness for efficient treatment include application without fingertip, immediate onset of action, reduced dosage regimen and economy. tulasi[3-5] a herbal medication has anti bacterial and anti fungal activity commonly used in the treatment of several skin disorders as it is not available in such dosage form.[6-7]. Objective of the present work was to develop such a NDDS of prepare Tulasi medicated derma sticks by heating and congealing method .

II. MATERIALS AND METHODS

Tulasi was gift sample from Euro drug Laboratory., Hyderabad., T.S. Stearyl alcohol pure, white petrolatum (Loba chemie Pvt. Ltd., Mumbai), Sodium lauryl sulphate, Cetyl Alcohol (S.D. fine chemicals ltd. Mumbai), Propylene glycol (Ranbaxy lab. Ltd., SAS Nagar), Methanol (Qualigens Fine Chemicals, Mumbai) were used.

Preparation of medicated derma sticks of Tulasi. Medicated derma sticks were prepared by heating and congealing according to the formulae (Table 1). Depending upon the weight, thickness and length of medicated derma sticks, the formulae was chosen for the incorporation of the drug. Stearyl alcohol[8] / Cetyl alcohol[9] and white petroleum were melted in a china dish and heated this mixture up to 70^0C. Dissolve sodium lauryl sulfate, propylene glycol in purified water and heat the solution to 70^0C separately. Add the oleaginous phase slowly to the aqueous phase, stirring constantly and then the drug was added slowly with continuous stirring in order to get a uniform mixture in optimized formulation. The hot mixture was poured into the glass mould and cooled to get the desired shape of sticks. The stick was removed from the mould after 24 hours with the help of plunger and inserted into the medicated derma stick container (Table 1)

Evaluation of prepared medicated derma sticks: Three sticks were selected randomly and weighed individually. The individual weights were compared with the average weight for determination of weight variation. As the shape of the stick is cylindrical the thickness and length was determined with the help of screw gauge and vernier callipers respectively. The average thickness was measured, by observing thickness at three different parts of the stick. (Table 2)

Anti microbial studies of prepared formulations[10]: The anti microbial studies were carried out for the prepared formulations by cup-plate method using *Candida Albicans* as test organism. The cultures of Candida albicans were cultivated on Sabouraud's dextrose agar maintained on slants in the refrigerator (4±2ºC).Table 4)

Cup-plate method: The composition of Sabouraud's dextrose agar was taken in a 250 ml of conical flask and was dissolved in 100 ml of distilled water. The pH was adjusted to 5.6. The medium was sterilized in an autoclave at 15 lbs for 20 minutes.After the completion of sterilization, the medium was kept aside at room temperature. 0.5 ml diluted suspension culture in NaCl 0.9% were added to 100 ml of medium at 47±2ºC and used as inoculated layer. The medium (20 ml) was poured into a sterilized petridish to give a depth of 3-4 mm, and was assured that the layer of medium is uniform in thickness by placing petridish on a leveled surface. After solidifying the medium at room temperature, with the help of a sterile cork borer, cups of each 6 mm diameter were punched and scooped out from the petridish. Using sterile pipettes sample solutions (0.1 ml) of known concentration were fed into the cup. The petridish was then incubated for 24 hours at 37ºC. After incubation the zone of inhibition was measured.

Preclinical studies: Primary skin irritation test in animals: This test is conducted on 3 healthy rabbits and guinea pigs (2 male and 1 female), which were fed with fresh food and water during the test period. 24 hours prior to test, the hair from the lower abdominal portion was shaved to expose sufficiently large test area. The test site was cleaned with surgical spirit then medicated stick is applied to test area. The test site was observed for erythematic and edema for 72 hrs. after application. This test was conducted to evaluate the irritancy of the prepared medicated stick on the intact skin of rabbits and guinea pigs.(Table 5,6)

Preclinical studies: Primary skin irritation test in healthy human being volunteers:: 3 Healthy Human Volunteers were selected for the study for each formulation. The test site was cleaned with surgical spirit then medicated stick is applied to test area. The test site was observed for erythema and edema for 24 hrs. 48 hrs. & 72 hrs after application. This test was conducted to evaluate the irritancy of the prepared medicated stick on the intact skin. None of the prepared medicated sticks showed any erythematic or edema, indicating that the prepared formulations were non-irritant on the skin. . These studies were carried out under the guidance of qualified dermatologists with the permission of ethical committee of M. R. Medical College, Gulbarga.(Table 7)

Stability Studies: Short-term stability studies on the promising formulation MP-1 were carried out by storing the sticks at 27±2°C for a period of three weeks. At intervals of one week the sticks were visually examined for any physical changes.(Table 3)

III. RESULTS AND DISCUSION

Steryl alcohol and Cetyl alcohol as stiffening agent while petrolatum used as emollient, propylene glycol and sodium lauryl sulphate were used as humectants and emulsifying agent respectively. A total of six formulations were designed. As the material was uniformly filled in mould with uniform Medicated sticks of Tulasi were prepared by heating and congealing method.. the sticks obtained were of uniform length, thickness and weight respectively. Antimicrobial studies revealed that the drug in formulation show equal zone of inhibition like pure drug . The preclinical studies in animals and healthy human volunteer revealed that the prepared formulations will be safe to use for topical applications (Fig 1 to4)

IV. CONCLUSIONS

The present work is a unique piece of contribution to the drug industry. The results will be useful to industry R&D for further investigations. The continuation of these work clinical studies is in progress.

V. ACKNOWLEDGEMENTS

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Table No. 1: Formula of medicated derma stick

Sl. No.	Ingredients	Quantity in gms.
1.	Tulasi powder	1.00
2.	Stearyl alcohol	15.00
3.	White petrolatum	20.00
4.	White Beeswax	5.00
5.	Sodium lauryl sulfate	1.50
6.	Propylene glycol	12.50
7.	Purified water (Q.S.)	100.00

Table No. 2: Comparative data of weight, thickness and length of medicated derma sticks

Formulation code	Medicated stick		
	Weight (gm)	Thickness (mm)	Length (cm)
	Mean ± SD	Mean ± SD	Mean ± SD
Tulasi	1.61 ± 0.03	6.34 ± 0.03	4.0 ± 0.01
Tulasi	1.61 ± 0.03	6.34 ± 0.03	4.0 ± 0.01
Tulasi	1.61 ± 0.03	6.34 ± 0.03	4.0 ± 0.01

Each reading is a mean of three determinations

Table No. 3: Stability studies of Tulasi derma sticks

Storage temperature	Time of analysis	Physical appearance	pH	

	(days)			
	15	No change	7.1	
	30	No change	7.0	
	45	No change	7.0	
	60	No change	7.1	
	75	No change	7.0	
	90	No change	7.0	
	105	No change	7.1	
	120	No change	7.0	
	135	No change	7.0	
At room temperature	150	No change	7.1	
$27 \pm 2^{o}C$	165	No change	7.0	
	180	No change	6.9	

Each reading is a mean of three determinations

Figure -1: Antimicrobial Studies Showing The Comparative Zone Of Inhibition Of Drug As Pure And In Formulation Tulasi

Pure drug

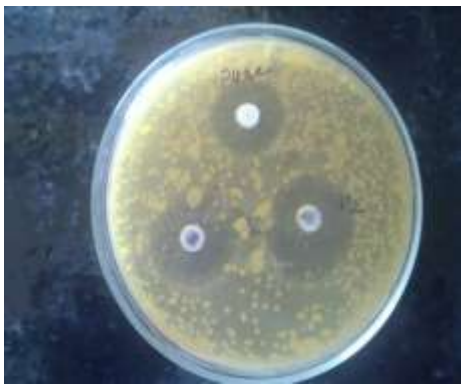

Plate-3

Pure drug

Plate-2

Pure drug

Plate-3

Table 4 : Antimicrobial Studies Showing The Comparative Zone Of Inhibition Of Drug As Pure And In Formulation Tulasi

Formulation code	Statistical zone of inhibition (mm) after 36 hrs			Mean ± S.D.
	Zone 1	Zone 2	Zone 3	
Pure Drug	22	23	24	22.65±0.56
Tulasi (Plate-1)	22	21	21	21.32±1.51
Tulasi (Plate-2)	20	22	20	20.65±1.14
Tulasi (Plate-3)	21	20	22	21.00±1.51

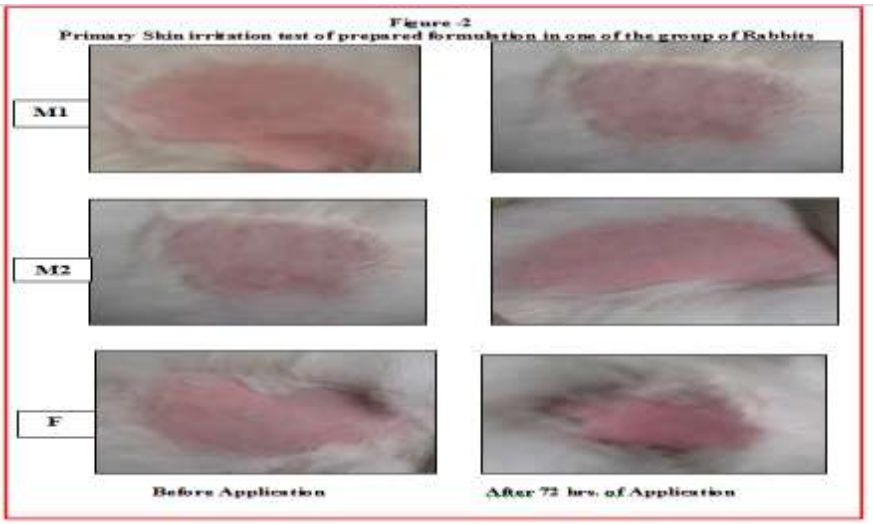

Table No-5 Skin Irritation Test Data Of Prepared Derma Stick Bases For Rabbits

Formulation code	Rabbits	Before application			After 24 hrs. of application			After 48 hrs. of application			After 72 hrs. of application		
		I	R	E	I	R	E	I	R	E	I	R	E
Tulasi	Male-I	x	x	x	x	x	x	x	x	x	x	x	x
	Male-II	x	x	x	x	x	x	x	x	x	x	x	x
	Female	x	x	x	x	x	x	x	x	x	x	x	x

I- Skin irritation,
R- Redness,
E- Erythema

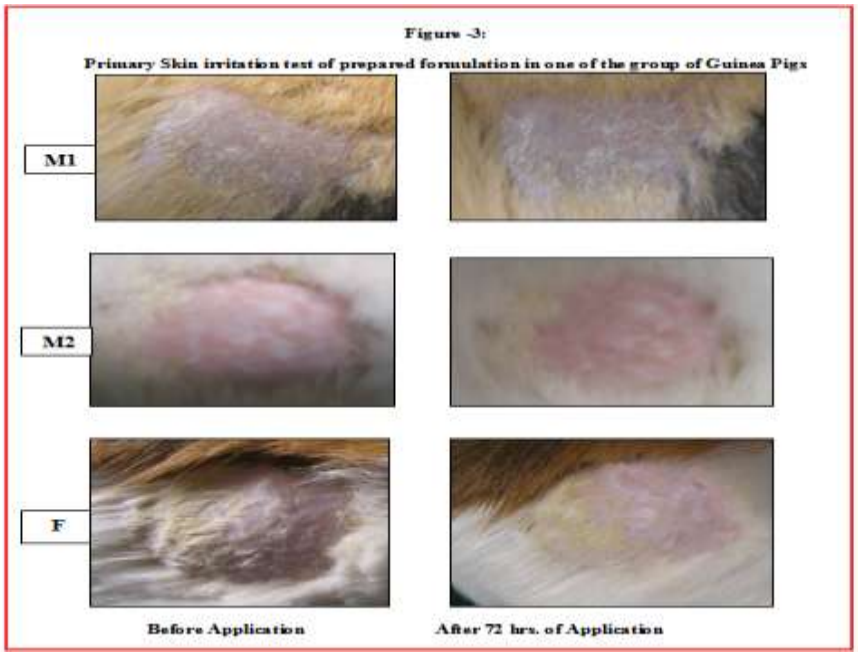

Table No. -6 Skin irritation test data of prepared derma stick bases for Guinea pigs

Formulation code	Guinea pigs	Before application			After 24 hrs. of application			After 48 hrs. of application			After 72 hrs. of application		
		I	R	E	I	R	E	I	R	E	I	R	E
Tulasi	Male-I	x	x	x	x	X	x	x	x	x	x	x	x
	Male-II	x	x	x	x	X	x	x	x	x	x	x	x
	Female	x	x	x	x	X	x	x	x	x	x	x	x

I- Skin irritation
R-Redness
E-Erythema

Figure-4: Primary Skin Irritation Test of prepared formulation in Healthy Human Volunteers

Table No.-7 Skin irritation test data of prepared derma stick bases for Healthy Human Volunteers

Formulation code	Human Volunteers	Before application			After 24 hrs. of application			After 48 hrs. of application			After 72 hrs. of application		
		I	R	E	I	R	E	I	R	E	I	R	E
Tulasi	Male-I	x	x	x	x	x	x	x	x	x	x	x	x
	Male-II	x	x	x	x	x	x	x	x	x	x	x	x
	Female	x	x	x	x	x	x	x	x	x	x	x	x

I-Skin irritation
R-Redness
E-Erythema