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PREPARATION AND DEVELOPMENT OF A TOPICAL FILM-FORMING GEL CONTAINING EXTRACTS OF GARLIC, ASHWAGANDHA AND TURMERIC FOR THE TREATMENT OF ACNE

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Abstract

The objective of the present study was to prepare a topical film-forming gel for the treatment of acne containing Garlic, Ashwagandha and Turmeric extract, using a patient-friendly drug delivery method. The localized cure of disease of our body tissues requires that the pharmaceutical active ingredient to be maintained at the site of treatment for some period of time. Sweat, garments and actions are some of the problems that have limited the helpfulness and residence time of conventional topical formulations mainly used for treatment of acne.

Common human skin disease is acne vulgaris which is characterized by areas of skin with seborrhea, comedones, nodules (large papules), and pimples and possibly scarring. Herbal formulations have been constantly growing and important in the world market. The present formulation deals with the preparation and development of the herbal film forming anti-acne gel containing hydroalcoholic extract of Garlic (*Allium sativum L*., Alliaceae), Ashwagandha (*withania somnifera*) and Turmeric (*Curcuma longa)* extract which is known for its anti-oxidant, anti-microbial & anti-inflammatory property. Various formulation batches i.e. S_1 to S_4 were formulated & evaluated for different parameters like color, appearance, consistency, pH, spreadability, antimicrobial activity & in vitro drug release. The formulation S_3 with maximum spreadability & antimicrobial activity was selected as the optimized formulation. Antimicrobial activity was compared with the marketed formulation.

Key words**:** - Film forming gel, Garlic, Ashwagandha, Turmeric, Anti- acne, Antimicrobial activity, Formulations.

1. INTRODUCTION

Film-forming gels are the drug delivery systems which have newly been used to deliver a variety of drugs to the skin as another to conventional topical and transdermal formulations. These systems consist of film-forming polymers in a vehicle & drug, which on application to the skin surface forms a thin, transparent film on solvent evaporation. Compared to conventional semi-solid topical products like ointments and gels, film-forming gels in addition to their therapeutic effect are esthetically more attractive to the patients. They are non-sticky, get adhered to the affected part for a longer period without getting rubbed off and can be designed to provide sustained drug release such that frequent reapplication is not necessary. All these give attractive properties which can develop patient compliance.[1]

Acne is one of the most common multifactorial chronic inflammatory diseases of the pilosebaceous follicles involving altered follicular keratinization; androgen induced sebaceous hyperplasia, hormonal imbalance, immune hypersensitivity & bacteria (Propionibacterium acnes) colonization. P. acnes are an anaerobic Gram-positive bacterium that makes propionic & acetic acid. These bacteria are involved in the development of inflammatory acne by activating complements and metabolizing sebaceous triglycerides into fatty acids that put out the follicular wall and surrounding dermis. It also produces exoenzymes & chemotactically attracts neutrophils[2]. Traditional herbal medicines provide an interesting and unexplored source for the anti-acne development, such as garlic (*Allium sativum*), Ashwagandha (*Withania Somnifera)* and Turmeric (*Curcuma longa)*.

Allicin (diallyl thiosulfinate or diallyldisulfide) is the most biologically active compounds in garlic and Alliin (S-allylcysteine sulfoxide) is the most abundant sulfur compound in garlic. Although allicin is considered the main antioxidant & scavenging compound. Garlic is very useful effect on acne due to anti-inflammatory, anti-microbial & anti-oxidant activities of different chemical constituents.[3]

Withania somnifera known commonly as ashwagandha, Indian ginseng, poison gooseberry, is an annual evergreen shrub in the Solanaceae or nightshade family that grows in India, the Middle East & parts of Africa. It is a well-known medicinal plant in Ayurvedic medicine. The principle active compounds include several withanolide type compounds. For the nontoxic & high medicinal value of *W. somnifera*, it is widely used as a home remedy for numerous diseases. The roots of the plants are also known for its antimicrobial activity apart from adaptogenic, anti-inflammatory & stress relieving properties.[4]

The turmeric has been used as a non toxic drug in ayurveda for treatment of various diseases including skin diseases, inflammation hepatic disorders etc. The plant selected for present work are curcumin longa which contain the high percentage of flavonoids & also responsible for anti-inflammatory activity. The herbal medicines are more accepted in the world for their lesser side effects & low cost. It has great significance for nutritional & heath benefits. It plays an important role in health benefit.[5]

Figure 1:- Garlic

Figure 2:- Ashwagandha

Figure 3:- Turmeric

2. MATERIAL & METHOD

2.1 Materials

The chemical were used hydroxyl propyl methyl cellulose & polyvinyl pyrrolidone polymeric blend in different concentrations, polyethylene glycol 400 (PEG 400) as plasticizer & ethanol as solvent. Collection of plant Garlic scales, Ashwagandha root & Turmeric powder were collected from the local market of Solapur.

2.2 Methods

2.2.1 Extraction of garlic

Garlic scales were cut into small pieces, dried in darkness and grinded to formulate fine powder. 50gm of herbal drug were taken & added to the conical flask containing 5 times volume of 1:1 water-

ethanol mixture. The contents were boiling on water bath under reflux condition for about 30 min. The contents were filtered and solid residues were once again boiled with five times volume of 1:1 water-ethanol mixture in the water bath under reflux condition for about 15 min. The contents were filtered out and filtrates were combined. Filtrate was dried on water bath until the desired concentration of the extract was obtained.[6]

Figure 4:- Simple extraction process

Figure 5:- Drying of filtrate

2.2.2 Extraction of ashwagandha

Ashwagandha root were grind to make fine powder and Ashwagandha powder was subjected to maceration with methanol. A mixture of ashwagandha and methanol in ratio 1:2 (w/v) was carried out using methanol. 100gm of crushed ashwagandha root was soaked in 200ml of methanol for 7 days. After 7 days mixture should be filtered using muslin cloth and take residue & dry it in room temperature.

2.2.3 Extraction of turmeric

Turmeric powder was subjected to maceration with methanol. A mixture of Turmeric and methanol in ratio 1:2 (w/v) was carried out using methanol. Turmeric powder was soaked in 200ml of methanol for 2 days. After 2 days mixture should be filtered using muslin cloth and take residue & dry it in room temperature.

2.2.4 Preparation of gel

The polymeric solutions of Polyvinyl Pyrrolidone & Hydroxy propyl methyl cellulose in ethanol were prepared using dispersion method. Polyvinyl pyrrolidone was spread over 30 ml of ethanol containing PEG 400 (3 % v/v). Hydroxy propyl methyl cellulose was spread over 30 ml of ethanol separately. The polymeric solutions were mixed appropriately with continuous stirring. Accurately weighed quantity (1gm, 1.5gm & 0.5gm) of the Garlic, Ashwagandha and Turmeric extract respectively was dissolved in 30 ml ethanol. The drug solution and polymeric dispersion were mixed with continuous stirring & the pH was adjusted with triethanolamine solution. Finally the volume was made up to the mark by ethanol.

Table 1 Formulation of garlic & ashwagandha film forming gel

Ingredients	S_1	S_2	S_3	S_4
Garlic Extract(g)	1	1	1	1
Ashwagandha(g)	1.5	1.5	1.5	1.5
Turmeric(g)	0.5	0.5	0.5	0.5
PVP (g)	8	8	10	10
HPMC (g)	8	10	8	10
PEG 400(mL)	5	5	5	5
TEA (mL)	12	12	12	12
Ethanol(mL)	100	100	100	100
Methyl paraben(mg)	100	100	100	100

PVP: - Polyvinyl Pyrrolidone, HPMC: - Hydroxy Propyl Methyl Cellulose, PEG: - Polyethylene glycol 400

3. EVALUATION OF FILM FORMING GEL

3.1 Physical appearance & pH of film-forming gel

The texture, appearance & transparency of the gels were examined visually. The pH value of film-forming gels formulations were evaluated by using calibrated digital pH meter. 1 gm of gel was dissolved in 100 ml of distilled water and kept for 2 hours. The measurement of pH of each formulation was performed in 3 times and the mean values were calculated.[7]

3.2 Drying time

One gram of the gel was placed on a petri dish which was spread uniformly on petri dish and kept on a hot plate at 37˚C and time needed until gel dry.[8]

3.3 Irritancy

Small amount of gel was placed on the skin kept for few minute and it was non-irritant.

3.4 Spreadability

The spread ability of the prepared gel was determined by measuring the spreading diameter of 0.5 g of gel in between two horizontal smooth surface glass plates (20 cm × 20 cm). The initial diameter of the spreading of the gel in centimeter was formed by put the gel on the glass plate was noted. Another glass plate with the same dimensions was placed over the gel for 1 min until no more expansion of the gel was observed. The upper plate was gradually removed & diameter of the circle formed after spreading of the gel was measured in centimeters.[9]

3.5 Antimicrobial study

Experiments were prepared in microbiology laboratory. Different antibacterial activities of formulations were measured by modified agar well diffusion method. In this method, nutrient agar plates of 0.2 ml of 24 hr. broth culture of S. aureus were seeded. The agar plates were solidifying and a sterile borer was used to cut wells of equidistance in each of the plates. Small amount of Garlic, Ashwagandha formulation & marketed clindamycin gel were introduced into the wells. The plates were incubated overnight at 37°C for 24hrs. The antibacterial activities were evaluated and zones of inhibition were studied in mm. [10-11]

3.6 In vitro drug release study (Diffusion study)

Franz diffusion cell were used to study the release profile of drug from film forming gel. The cell consists of two chambers it is the donor and the receptor compartment between in which a diffusion membrane was mounted. The donor compartment, of inner diameter is 24 mm. The diffusion medium used phosphate buffer solution pH was 5.8. 1 mL of the drug containing film forming gel was located 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 24 hours in phosphate buffer solution. The donor and receptor compartments were attached together using a clamp. Whole assembly was placed on a magnetic stirrer. The receptor compartment with 100 mL of phosphate buffer solution was placed on magnetic stirrer. It was maintained at 37 ± 0.5^0 C and stirred continuously at 50 rpm. Samples of 1 mL were collected at predetermined time intervals & analyzed for drug content by UV Spectrophotometer at λ max against blank. The receptor phase was replaced with an equal volume of phosphate buffer at each time of sample withdrawal[12-13]

4. RESULT & DISCUSSION:-

4.1 Physical appearance & pH

The physical appearance of film forming gel was such as color & consistence were visually checked & shown in figure 6 & table 2. The pH value of gel formulation is shown in table 3. Gel were found to be in the range of 8.4 - 8.6 slightly alkaline pH which has compatible with normal skin.

Figure 6 Film forming gel formulation

Table 2

Formulation code	Color	Consistency
S_1	Light yellow	Semi-solid
S_2	Light yellow	Semi-solid
S_3	Light yellow	Semi-solid
S_4	Light yellow	Semi-solid

Table 3 Determination of pH

Formulation code	P^H
S_1	8.5 ± 0.2
S_2	8.4 ± 0.2
S_3	8.5 ± 0.2
S_4	8.6 ± 0.2

4.2 Determination of drying time

The drying time of all the formulations were found to be in between 185 sec to 230 sec.

Table 4 Determination of drying time

Formulation code	Drying time
S_1	185sec
S_2	210sec
S_3	200sec
S_4	230sec

4.3 Determination of Spreadability

The spread ability tests were carried out between 5.4± 0.2 & 6.2 ± 0.2 cm. This indicates the spread ability increased with decrease in polymer concentration.

Table 5 Determination of Spreadability

Formulation code	Spreadability(cm)
S_1	6.0 ±0.2
S_2	5.4±0.2
S_3	6.2±0.2
S_4	5.8±0.2

4.4 Determination of antimicrobial activity

The gel formulation were showed considerable zone of microbial inhibition compare with standard clindamycin drug. In comparative study formulation S3 showed more antimicrobial activity than other formulation.

Figure 7 Antimicrobial study

S1, S2, S3, S4= Antimicrobial activity of Formulation A= standard drug (clindamycin)

Table 6 Anti acne activity

Formulation code	Zone of inhibition (mm)
A	4
S_1	4.5
S_2	5.1
S_3	6
S_4	3.9

Table 7 Cumulative % release of drug

Time in h.	Cumulative % release of drug			
	S_1	S_2	S_3	S_4
0	0	0	0	0
1	21.40	23.48	28.00	24.20
2	32.00	35.55	38.01	37.09
3	43.94	45.70	45.09	41.09
4	57.11	58.07	59.66	59.01
5	71.77	75.86	76.84	75.95
6	80.77	85.86	86.00	83.89

5. CONCLUSION

In the world market, now a days, herbal gel formulation have growing demand & it is very good attempt to create the herbal gel containing extract of garlic, ashwagandha & turmeric for the treatment of acne. Formulation S_1 to S_4 was semi solid consistency. All the formulation was very slightly alkaline pH which has been compatible with normal skin physiology. Formulation S_1 & S_3 had very optimum drying time & S_3 optimum spread ability. All the formulation showed considerable zone of microbial inhibition compare with standard drug clindamycin. Formulation S_3 showed comparatively more antimicrobial activity than other formulation. The same formulation also showed highest percentage of drug release. Based on the results we conclude that the prepared formulation can be effectively used for treatment of acne.

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