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Research Article

Formulation and Evaluation of Topical Spray Containing Anti Acne Agent

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ABSTRACT

Objective: The objective of the present study was to formulate a novel topical spray containing Antiacne agent. Comprising drug and other non-toxic excipients (mixture of propane and butane) LPG as propellant. Study was designed to increase the absorption of drug from the human skin. Therefore clear clinical need exists for development of suitable formulation of drug that has improved permeability and absorption, with the potential transparent thin film with the once daily dosing. An optimum formulation was to be study for skin irritation study, *in-vivo* drug release and finally for stability study.

Experimental work: The preformulation studies for drug was carried out and compatibility of drug in formulation with different excipients was checked. Solutions for topical sprays were filled in Aluminium containers fitted with continuous spray valve. Primary screening of variables like polymers, penetration enhancers and solvents were done by preparing trial batches. Final batches were prepared comprising of polymer Eudragit E100 (flim forming polymer), penetration enhancers such as IPM and PG act as plasticizer, solvent and co-solvent such as Iso Propyl alcohol and ethanol respectively. Prepared Tazarotene topical spray formulations were evaluated for different parameters. Tazarotene topical spray included determination of delivery rate, delivery amount, pressure test, drug content, minimum fill, leakage test, flammability, spray patterns, particles size, etc and as well as *In-vivo* Skin irritation study and In-vitro drug released, Finally, optimised formulation Was kept for stability study as per ICH guidelines.

Results and discussion: Absence of physical and chemical incompatibility during compatibility study revealed that Tazarotene is compatible with container closure and excipients. Tazarotene topical spray formulation T6 was found to be the best formulation Evaluation data of different formulation for Physico-chemical test, performance test and *ex-vivo* diffusion studies indicated the effectiveness of IPM as penetration enhancer. T6 was further proved non irritant and stability study in accordance with ICH guidelines indicated that the optimised formulation was stable.

Conclusions: A novel type of formulation comprised of Tazarotene, Eudragit E100, IPM and organic volatile and non-volatile solvents, was used to develop a new topical spray formulation. This novel topical spray formulation was transparent solution with good, early evaporation and ease of application. In addition the research results showed the resultant invisible thin film with excellent carrier and permeability enhanced effect of IPM on drug. Finally, skin irritation test proved that the spray formulation was safe to be used for topical delivery. In summary, the novel formulation of Tazarotene, Eudragit E100, IPM and other excipients may provide alternate dosage form to Tazarotene gel formulation.

Key-words:. Topical spray, Tazarotene Aerosol, Eudragit E100, Thin film.

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INTRODUCTION:-

Acne is a chronic inflammatory disease of the pilosebaceous unit resulting from androgen-induced increased sebum production, altered keratinisation, inflammation, and bacterial colonisation of hair follicles on the face, neck, chest, and back by *Propionibacterium acnes*. Although early colonisation with *P acnes* and family history might have important roles in the disease, exactly what triggers acne and how treatment affects the course of the disease remain unclear. Other factors such as diet have been implicated, but not proven. Facial scarring due to acne affects up to 20% of teenagers. Acne can persist into adulthood, with detrimental effects on Self-esteem.[1]

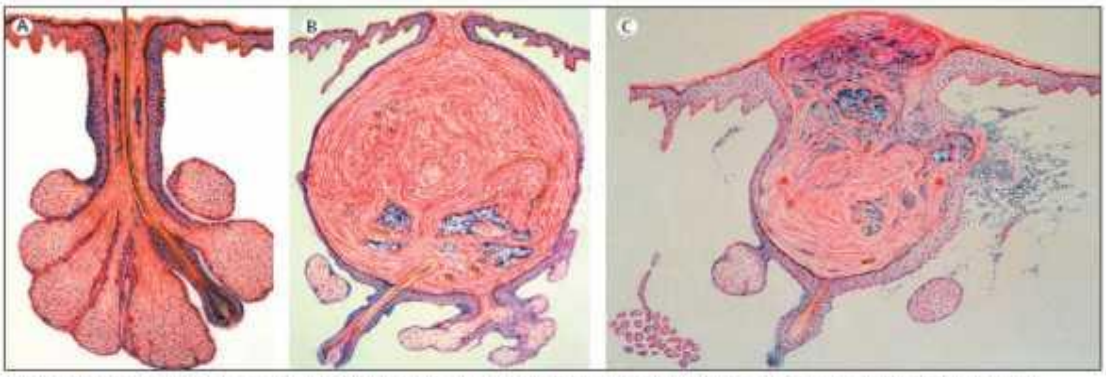


Figure 1: Normal sebaceous follicle (A) and comedo (B), and inflammatory acne lesion with rupture of follicular wall and secondary inflammation (C)

Figure No.1:-(A)Normal sebacaceous follicle (B)comedo (C)inflammatory acne lesion

- **CONVNTIONAL DOSAGE FORM**

For the treatment of Acne are 0.05% Tretinoin Solution, 0.05% Tretinoin Gel, 0.1% Tazarotene Cream , 0.1% Adapalene Gel, 2.5% & 5% Benzoyl peroxide Gel, 2% Erythromycin ointment & lotion, 1% clindamycin Gel, 10% Azelaic acid Cream.[3]

- **DISADVANTAGES OF CONVENTIONAL DOSAGE FORM**

- They are very sticky in nature so cause uneasiness to the patient when applied,
- Lesser spreading coefficient and need to apply with rubbing,
- Gels have limitation for delivery of hydrophobic drugs,
- Problem with stability,
- Difficulty in maintaining sterility,
- Mechanical application of conventional dosage form on acne produces irritation.

To overcome the limitations of the conventional dosage forms, spray or aerosol dosage form for topical application have been formulated. Topical aerosols are products that are packaged under pressure. The active ingredients are released in the form of fine liquid droplets or fine powder particles upon activation of an appropriate valve system.

- **NEED FOR STUDY**

Tazarotene is used as superficial anti-acne agent is selected as model drug candidate to formulate anti-acne topical spray. Absorption of Tazarotene through human skin is low. Less than 6.0% of the dose is absorbed during the followings 10 hours of topical administration [4].

"***Therefore clear clinical need exists for development of suitable formulation of Tazarotene that has improved permeability and absorption, with the potential transparent thin film with the once daily dosing.***"

It is hypothesized that the topical spray dosage form would deliver the bioactive compound directly to the infected area and produce a film that would cover the infection and act as reservoir for the bioactive drug. This would also minimize the pain irritation during application.

- **Drug delivery system**
  - **Introduction of topical spray:**

1. Physical, chemical, and pharmacologic properties of active ingredients.
2. Site of application.

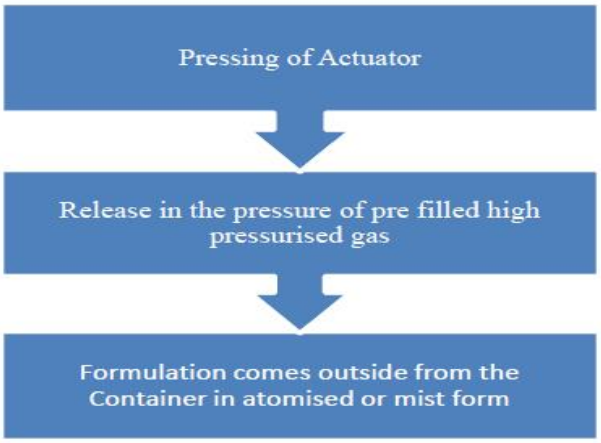
Different types of Aerosol systems	
Solution system	Two-phase system- vapour and liquid phase. When the active Ingredients are soluble in the propellant, no other solvent is required.
Water-Based System	Three-phase system- propellant, water, and vapour Large amount of water can be used to replace all or a part of the nonaqueous solvents.
Suspension or Dispersion System	Dispersion of active ingredients in the propellant or a mixture of propellants. To decrease the rate of settling of the dispersed particles, various surfactants or suspending agents have been added.
Foam system	Consists of active ingredients, aqueous or nonaqueous vehicles, Surfactant, and propellant and are dispensed as stable or quick- breaking foam. The liquefied propellant is emulsified and is generally found in the internal phase.

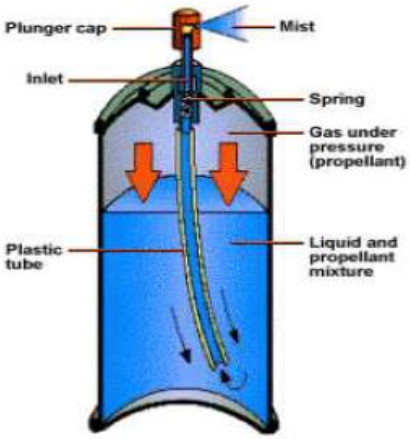
Table No.1:- Different types of Aerosol systems

- **Advantages Topical Spray:**

1) Dose can be delivered without contamination without contamination of Entire product.
2) Sterility can be maintained if required.
3) No need of any mechanical means for application.
4) Easy to use with better patient compliance.
5) Medication can be delivered directly at the site of action in desire form i.e. Spray, Foam etc
6) Covers very small area of skin.
7) Cannot be even seen or event felt after application.
8) Avoidance of first pass metabolism.
9) Avoidance of the risks and inconvenience of intravenous therapy and of varied condition of absorption like ph changes, presence of enzymes, gastric emptying time, Etc.
10) Avoid fluctuation in drug levels, inter and intra patients variations.
11) Ability to deliver drug more selectively to specific site.
12) A relatively large area of application.
13) Avoidance of gastro-intestinal incompatibility.
14) Provide suitability for self-medication.

- **Mechanism of spray:**
  - ✓ Spray mechanism at the time of actuation is explained diagrammatically in the figure.
  - ✓ Release in the interior pressure of the propellant leads to atomization of the formulation filled in the container.





- **AIM AND OBJECTIVES**
- **AIM**

The aim of present work is to formulate & evaluate **topical spray** containing **Antiacne agent.**

- **OBJECTIVES**

To meet the above mentioned aim the following objectives are undertaken:

1. Development and optimization of spray solution for characteristics like **pH, viscosity, drug content, film formation** etc.
2. To study effect of **penetration enhancer** on permeation rate of Tazarotene.
3. To carry out **compatibility study** of drug (Tazarotene) with the container and other solvents.
4. To study **ex-vivo drug release** study of Tazarotene topical spray.
5. To study **skin irritation study** of optimized Tazarotene topical spray using Selected animal model.
6. Evaluation **of topical spray** system.

- **RATIONALE OF PROPOSED WORK**

- Various conventional formulations like gels, creams, ointment, etc. are available in the market for topical administration but they have shortcomings like risks of contamination, tackiness, sticky nature causing uneasiness to patient when applied.
- While using topical spray compensates these defects.
- Medication is dispensed to the push of a button.
- The medication can be delivering directly to the affected area in a desired form, such as spray, stream, quick breaking-foam, or stable foam.
- A portion of medication can be easily withdrawn without contaminating the remaining material.
- Sterility can be maintained throughout the product's shelf life.
- Irritation is produced by mechanical application of topical medicament is reduced or eliminated.
- The active drug is protected from oxygen and moisture.
- The spray formulation gives faster onset of action.
- Topical formulation is more convenient and patient friendly.
- Formulation can be delivered multiple times without contamination.
- Hermetically sealed container allows integrity throughout the use of product.
- Single phase solution is formulated such that a volatile component evaporates, leaving behind a concentrated solution of drug in a carrier that is rapidly taken up by outer layer of the skin avoiding the first pass metabolism and GIT irritation.

- **Preparation of preliminary batches:** Batches were prepared by using polymers like Eudragit E100, PVP K30 and combination of Eudragit E100 and PVP K30 (1:1). All the variables like concentration of drug, PG, IPA and IPM were kept constant. Table shows the composition of preliminary batches. These batches were studied for drug release.

Table No.2:- Composition of trial batches

Batch code	Polymer Used	Polymer concentration	Drug (mg)	IPA (ml)	PG (ml)	IPM (ml)	Ethanol
A1	PVPK30	0.5%	20	1.25	1.5	0.5	16.45
A2		0.75%	20	1.25	1.5	0.5	16.40
A3		1.0%	20	1.25	1.5	0.5	16.35
A4	Eudragit E 100	0.5%	20	1.25	1.5	0.5	16.45
A5		0.75%	20	1.25	1.5	0.5	16.40
A4		1.0%	20	1.25	1.5	0.5	16.35
A7	Eudragit E 100 + PVP K30 (1:1)	0.5%	20	1.25	1.5	0.5	16.45
A8		0.75%	20	1.25	1.5	0.5	16.40
A9		1.0%	20	1.25	1.5	0.5	16.35

- **Optimization of batches based on preliminary study:** From the Above preliminary study Eudragit E100 was selected as the polymer. For the further study the batch was selected as per Table no. 2. These batches were studied for drug release. Selections of batches for evaluation were selected on greater release profile of the batches.
- **EVALUATION OF TOPICAL SPRAY [20,22,23]:**
- **Evaluation of Physico-Chemical Characterization Topical spray:**
- **pH:**
  The pH of optimized solution of the spray was determined using digital pH meter. Before measuring the pH of optimized formulation, the pH meter was calibrated with the help of phosphate buffer pH 4.0, 7.0 and 9.0. Then about 30 ml of spray solution was taken in a small glass beaker and the electrode of pH meter was dipped into it for a minute and the pH was noted. The measurement of pH of each formulation was done in triplicate and mean values were calculated.
- **Viscosity:**
  Viscosity of solution for topical spray was determined by Oswald viscometer. 30 ml spray solution was filled in Oswald viscometer. Flow of solution was measured in time from A to B point in viscometer. Reading was taken at least three times. Viscosity of spray 1solution was measured against the viscosity of water [38].
- **Density:**
  Dried and emptied Pycnometer was weighed. The sample were filled in it and air bubble were allowed to rise to top before inserting the stopper. Pycnometer was handled by the neck with one or two layers of paper between the fingers and the bottle to avoid expansion due to the heat of the hand. The proper value of the density was known by dividing the resultant weight of liquid by its volume in Pycnometer.
- **Pressure test:**
  As per method described in USA at the temperature of 25^0C, Not fewer than four aerosol were selected each container is placed in an upright position. The actuator is pressed to remove liquid from the dip tube and valve. The actuator is removed and replaced with the pressure gauge. The gauge is pressed to actuate the valve and the pressure exerted by the propellant is being noted for each aerosol container with the help of

pressure gauge. Noted down the pressured gauge is measured [39].

Figure No.2:- Figure of pressure gauge.

- **Flame Projection:**
  This test indicates the effect of an aerosol formulation on the extension of an open flame. Product is sprayed for 4 sec. into flame. Depending on the nature of formulation, the fame is extended, and exact length will be measured with ruler. The sample is classified as flammable if ignition occurs at a distance equal or greater than 15 cm but less than 75 cm.

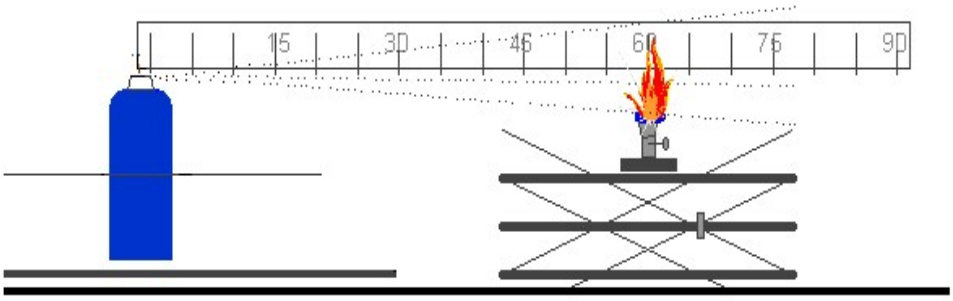


Figure No.3:-Flame Projection

➢ **Evaluation of Topical spray:**

- **Leak test:**
  Two types of leak test are being performed as described below.

1. Immediate leak test:

Filled aerosol containers are allowed to sink in warm water (around 50^0C) for
About 10 seconds, immediately after the filling. The bubbling in water is being identified as a leakage in the container.

2. Delayed leak test:

Accurately weighed aerosol containers are keeping at room temperature for 2 months. After this time period the containers are weighed again. The difference in the weight of a container is being identified as leakage in the container.

- **Spray angel:**
  First, the distance will be fixed between paper from nozzle. Then, one actuation is being sprayed on to paper and measured radius of the circle.
  Spray angle is being calculated from equation:
  Spray angle (□) =$\tan^{-1}$(1/R)
  Where 1 cm is distance of paper from the nozzle and R is average radius of the circle.

- **Spray patterns:**
  The formulation (one actuation) is sprayed on to pH sensitive paper which is prepared by dipping the whattman filter paper in the solution of methyl red. The distance separating the container from the target is keep constant at 5cm. Then, the spray pattern is being evaluated by spraying the concentrate in vertical position and in horizontal position. The maximum diameter (Dmax) and minimum diameter (Dmin) is noted. The ovality ratio is being calculated by ratio D max and $D_{min.}$ From this, it can be concluded that the spray pattern is uniformed or not
  Ovality ratio=D_{max}/D_{min}
  Where D_{min} and D_{max} are the maximum and minimum diameter of the spray pattern Respectively [10].

- **Delivery rate:**
  Delivery rate of spray is being evaluated according to the procedure stated in USP. Six aerosol containers are actuating for 5 seconds at a temperature 25^0 C and the average delivery rate is being calculated in gram per second [39].

- **Delivery amount:**
  Delivery amount is being determined by using six containers of spray according to procedure stated in USP. Valves are press continuously for 5 seconds each time and sufficient time was allowed between each actuation to avoid significant canister cooling. The total weight loss was calculated from each container as the deliverable amount [39].

- **Minimum fill of topical spray:**
  Five filled containers will be selected and weighed individually. The contents are removed from each container. The packages are opened and the residue is removed by washing with suitable solvents and rinsed with methanol. The container, the valve, and all associated parts were collected and heated to dryness at 100ºC for 5 minutes and cooled. The weight of each container together with their corresponding parts is determined. The difference between the weight of the filled container and the weight of the corresponding empty container is being the net weight of the content [39].

- **Particle size of Topical spray:**
  The particle size solution for spray of Tazarotene was determined by optical microscopy. Microscopic method are generally employed for measurement of particle size in range of 0.2 to 100. The particle sizes of optimized formulations were estimated. The formulation was sprayed on a clean glass slide and atleast sizes of 100 particles were measured under an optical microscope[41].

- **Drug content studies:**
  Remove of the all content from container actuating the valve. 1 ml spray for solution was taken in 10 ml volumetric flask containing 5 ml IPA and diluted upto 5ml with the same solvent. From the above solution, 1 ml was further diluted with 10 ml IPA. The resultant solution was filtered through Whatman filter paper and absorbance of the solution was measured at 233 nm using UV spectrophotometer.

- **Ex vivo skin permeation study:**
  Ex *vivo* skin permeation study is being performed by using Franz diffusion cells with an effective diffusion area of 2 cm^2. The excised skin samples (dorsal side) of Albino wistar rat (250gm-300gm) is clamped between the donor and the receptor compartment of Franz diffusion cells with the Stratum corneum facing the donor compartment. At predetermined time intervals, constant ml receptor medium is being withdrawn and the same volume of pure medium was immediately added into the receptor compartment. The procedure is repeated up to 24 h. All samples are analyzed by UV spectrophotometer [26,41].

- **Skin irritation study:**
As the formulation is being intended for dermal application, skin irritancy should be tested. Skin irritation tests are conducted at Albino rabbits (New Zealand white variety) to determine to determine irritancy after single application of Topical spray. Skin is being prepared by removing hair of the rabbit (backside) 24 hour before the control and test (Topical spray) application. The formulation is being sprayed on the patch of preshaved skin for 2 second and occluded with adhesive tapes and resulting reactions such as erythema and edema are scored after 24 h. The patch is being removed after 24 h and treatment sites are cleaned with wet gauze to remove any residual test substance. Exposed skin is being graded for formation of edema and erythema. Based on the scoring, the formulation is graded as 'non-irritant', 'irritant' and 'highly irritant'. Erythema and edema were graded as 0 for no visible reaction, 1 for just present reaction, 2 for slight reaction, 3 for moderate reaction and 4 for severe reaction. Eventually, the total scores for irritation test in each formulation are being calculated using the following equation [42-44].

$$\text{Primary irritation index} = \frac{(\text{Erythema reaction scores} + \text{Edema reaction scores})}{\text{Time interval (hr)}}$$

- **Stability studies:** Optimized formulation will be stored for the stability testing as per ICH guidelines "**Accelerated Stability Study**".[40]

Stability study	Temperature(^{0}C)	Humidity(%RH)	Time period
Accelerated Stability Study	40^{0}C±2^{0}C	75%RH±5%RH	20 Days

- **Result & Discussion:**

Table No.3:-In-Vitro drug release data of batches Preliminary batches B1 to B9.

Time (hr)	A1	A2	A3	A4	A5	A4	A7	A8	A9
1	**8.63**	**9.1**	**7.23**	**4.43**	1.4	1.16	**5.83**	3.26	1.69
2	**16.21**	**17.63**	**15.45**	**9.27**	7.28	4.48	**10.73**	8.53	5.45
3	**28.28**	**20.88**	**23.52**	**16.64**	15.04	12.35	**18.38**	15.86	14.84
4	**40.57**	**29.61**	**34.23**	**24.28**	22.4	18.67	**27.02**	23.01	19.01
5	**44.91**	**39.82**	**39.03**	**32.9**	30.25	24.76	**37.85**	31.12	32.14
6	**50.29**	**43.86**	**43.03**	**44.87**	38.39	31.29	**40.9**	36.72	37.87
7	**58.63**	**47.54**	**48.07**	**52.83**	46.11	34.78	**44.49**	40.4	42.36
8	**63.02**	**50.83**	**51.85**	**59.88**	52.68	37.43	**49.79**	43.47	44.46
24	**71.71**	**69.13**	**66.68**	**64.56**	57.82	54.6	**60.14**	57.34	55.8

➢ **Physico-Chemical Characterization of Topical Spray:**

- **pH:**
  pH was measured by using pH meter. 25ml Spray for solution was used to measure pH. The results are shown in table 4.

TableNo.4:- pH test data for A1, A2, A3, A4 and A7 batches.

Batch code	pH*
A1	7.09 ± 0.05
A2	7.10 ± 0.02
A3	7.19 ± 0.01
A4	7.20 ± 0.04
A7	7.15±0.02

*** Mean ± SD; n=3**

- **Viscosity:**
  Viscosity was measured by Oswald viscometer. Water was taken as reference solvent to measure viscosity. Flow of spray solution and water from A to B point were measured in time. The results of viscosity for topical sprays are shown in table 5.

Table No.5:-Viscosity data for A1, A2, A3, A4 and A7 batches.

Batch code	Viscosity (cps) *
A1	2.90 ± 0.43
A2	3.48± 0.37
A3	4.16± 0.45
A4	3.77± 0.25
A7	4.02±0.55

*** Mean ± SD; n=3**

- **Density:**
  Density was measured by the Pycnometer. Spray solution is used to measured the density. Reported density is given in the table 6.

Table No.6: Density data for A1, A2, A3, A4 and A7 batches.

Batch code	Density(gm/ml)*
A1	0.689±0.01
A2	0.679±0.02
A3	0.685±0.01
A4	0.688±0.01
A7	0.680±0.04

*** Mean ± SD; n=3**

- **Pressure test:**
  As all the formulas contain LPG as propellant, their vapour pressure was found in the range of 5.0 to 6.0 kg/cm2 when measured with pressure gauge.(1bar=14.51 psig)

Table No.7:- Pressure test data for A1, A2, A3 and A4 batches.

Batch code	Vapor Pressure (Bar) *
A1	5.45 ± 0. 05
A2	5.33 ± 0.03
A3	5.77± 0.05
A4	5.60±0.02
A7	5.55 ± 0.04

*** Mean ± SD; n=3**

- **Flammability and flame extension test :**
  Maximum flame extension was observed for A2 having highest vapour pressure.
  Flame flash back for all the formulations were found near about same which indicated the minimum leakage on spontaneous release of pressure for all five formulations.

Table No.8:- Observation table for Flammability test.

Formula	A1	A2	A3	A4	A7
Flame extension	66cm	77cm	70cm	69cm	75cm
Flash Back	10cm	12cm	13cm	10cm	10cm

➢ **EVALUATION OF TOPICAL SPRAY:**

- **Leakage test:** Leakage of canisters was confirmed by passing the canisters in water bath at 55°C temperature. Test was performed on selected batches. All batches were passed this test. No change in crimping dimension was found.

Table No.9:- Leakage test results of selected batches.

Batches	Result	
	Immediate	Delayed
A1	No leakage	No leakage
A2	No leakage	No leakage
A3	No leakage	No leakage
A4	No leakage	No leakage
A7	No leakage	No leakage

The leakage test for all aerosol containers was significantly different, but the results still met the requirement of USP. The product passed the average leakage test if the rate per year for the 12 containers is not more than 3.5% of the net fill weight.

- **Spray Angle:**

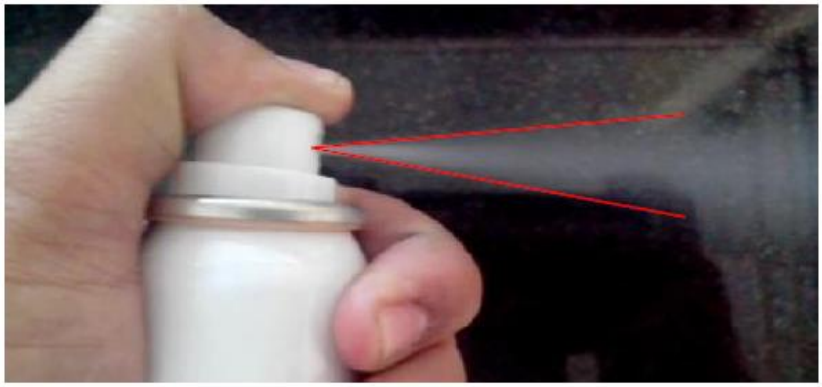


Figure No.4 :- Photograph for spray Angle:

Table No.10:- Observation table for Spray angle:

TEST	A1	A2	A3	A4	A7
Spray Angle	22 0	24 0	240	22 0	22 0

Furthermore the spray angle was found almost similar for all the trial batch formulation revealing the similar area of spray when applied topically.

- **Spray pattern:**
  Spray pattern was performed by using silica-gel glass plate method. Contents were sprayed on glass plate containing silica gel. The glass plates were analyzed under UV light to check spray pattern. The results of spray pattern of Tazarotene Topical spray are shown in figure.

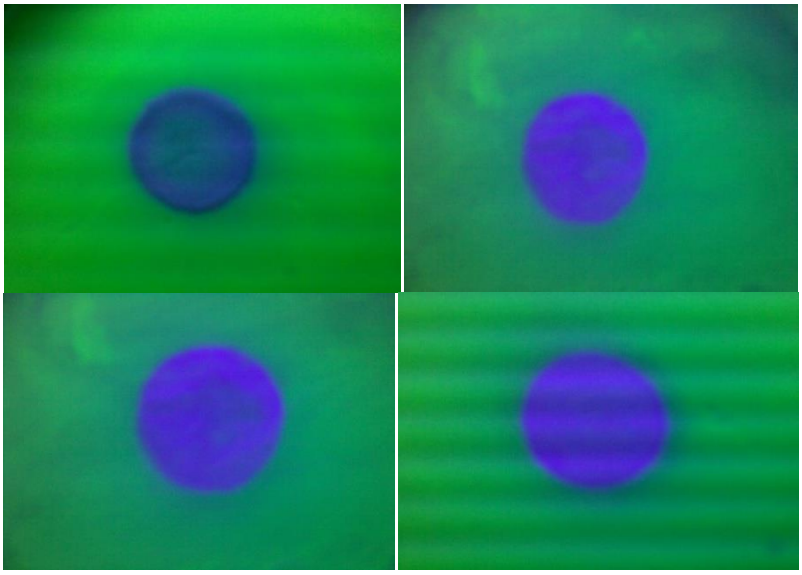


Figure No.5:- Spray pattern.

Table No.11:- Diameter of spray batches A1, A2, A3 and A4 batches.

Batches	Diameter (mm) *
A1	20 ±2
A2	18 ±3
A3	19±2
A4	18±1
A7	20±2

*** Mean ± SD; n=3**

- **Delivery amount and Delivery rate :**

Table No. 12:- Observation table for Delivery amount and Delivery rate test.

Formula	A1	A2	A3	A4	A7
Delivery amount (g/5 sec)	1.342	0.890	0.932	0.986	1.253
Delivery rate (g/sec)	0.255	0.116	0.186	0.197	0.250

- **Minimum fill:**
Ten filled containers were selected and weighed individually. The contents were removed from each container. After removal of contents was dismantle the container and rinsed with few portion of methanol. Parts of containers were dried at 100°C for 5 minutes and weighted to know net content. The results are shown in table 13.

Table No.13: -Minimum fill data for A1, A2, A3 and A4 batches.

Batch code	Minimum Fill (%)*
A1	100.85 ± 0.34
A2	100.17 ± 0.67
A3	100.42 ± 0.89
A4	100.42 ± 0.64
A7	100.33 ± 0.25

*** Mean ± SD; n=3**

The product passed the minimum fill test if the net weight of the contents is not less than the labeled amount. All formula had a minimum fill of more than 100 %, which mean that the net weight of the contents was not less than the labeled amount and met the requirement.

- **Particle Size of Topical Spray:**
By the optical microscopic method particle size measurement was determined. The reported result shown in table 14.

Table No.14: - Particle Size of Topical Spray data for A1, A2, A3 and A4 batches.

Batch code	Particle Size(µm)*
A1	8.6±2.24
A2	9.7±3.56
A3	11.39 ± 2.27
A4	11.68 ± 3.87
A7	8.5 ± 2.22

*** Mean ± SD; n=3**

- **Drug content:**
Removal of the solution from the container is about 1 ml was analyzed for the drug content by UV Spectrophotometer. The result shown in table 15.

Table No.15:-Particle Size of Topical Spray data for A1, A2, A3 and A4 batches.

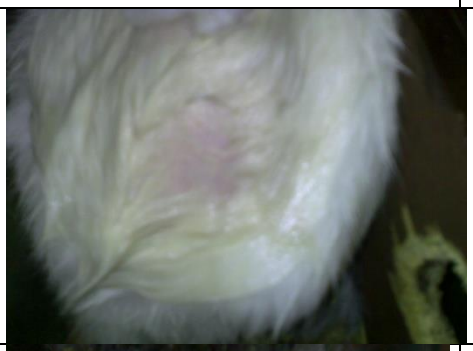
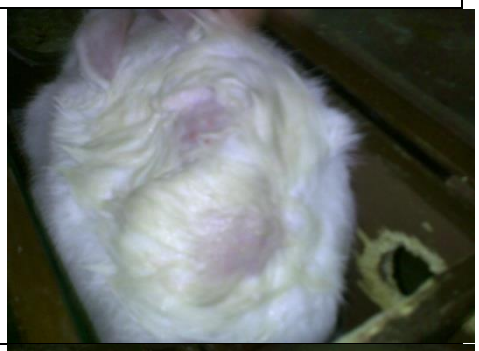
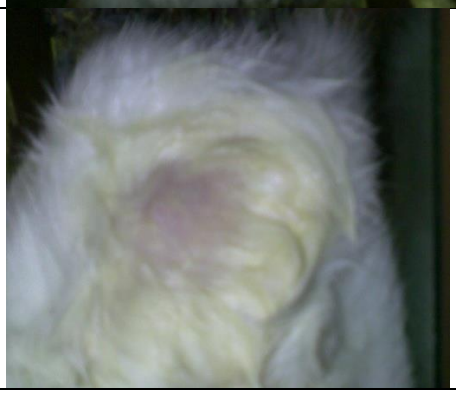
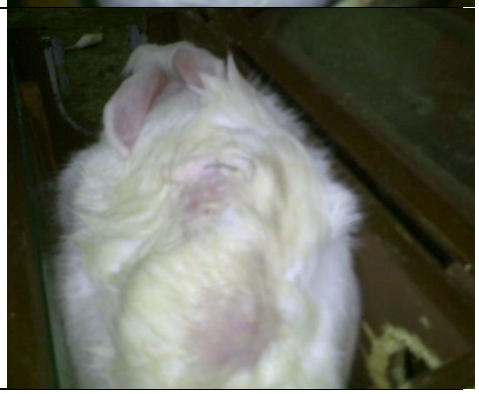
Batch code	Drug Content(%)*
A1	99.68±0.04
A2	99.87±0.05
A3	100.11 ± 0.02
A4	101.10 ± 0.01
A7	98.54 ± 0.03

*** Mean ± SD; n=3**

- **Skin irritation studies of the optimized Tazarotene topical spray:**

The results of skin irritation studies of the optimized Tazarotene topical spray are shown in table 16.

Table No.16:- Skin irritation studies of the optimized Itraconazole topical spray

Formulation	Before spray	After spray (24 hrs)
Control (Topical Spray Without Tazarotene)		
Test (Topical Spray Containing Tazarotene)		

- **Stability studies of Optimized batch as per ICH guidelines:**

Table No.16:- Observation table for Stability studies:

Sr. No.	Test	Parameter	At 40°C and 75%RH
1	Physico-chemical test	pH	7.10
		Viscosity	3.85 cps
		Density	0.689 gm/ml
		Pressure	5.65 bar
		Flame Extension	66 cm
		Flame Flash back	11 cm
2	Performance test	Spray Angel	23 ^{0}
		Spray Pattern	18 mm
		Delivery Rate	0.201 gm/sec
		Delivery Amount	1.102 gm/5 sec
		Drug Content	100.21%
		Particle Size	8.7 µm
3	Ex-vivo drug diffusion study	%CDR After 24 hrs	67.85%

➢ Conclusions

Acne vulgaris (simply acne) is a common human skin disease, characterized by areas of skin with seborrhea (scaly red skin), comedones (blackheads and whiteheads), papules (pinheads), pustules (pimples), nodules (large papules) and possibly scarring. Tazarotene formulations are available in lotion, cream, ointment and gel.
Tazarotene topical spray was formulated to overcome disadvantage associated with conventional dosage form like stickiness, lesser spreading coefficient and need to apply with rubbing. Irritation produced by mechanical application of topical medicament is reduced or eliminated by Tazarotene topical spray.
Tazarotene topical spray is applied with the push of button at the site of application without contaminating the remaining material. Topical spray of anti-acne agent is expected to form a clear transparent thin film at the site of application having property to adhere to the skin, as well as improved permeability and absorption thus effectively delivering the drug at the site of action, without pain or irritation.
Various polymers were chosen from solubility and preliminary batches study. From the preliminary batches study Eudragit E 100 polymer was selected on the basis of greater *in-vitro* release as well as solubility. Further optimization was done by altering the concentration of Eudragit E100, PG and IPA. Optimized batch containing higher concentration of PG and IPA with lower concentration of Eudragit E100 was found to give higher release of drug from formulation.
Tazarotene topical spray of optimized batches were evaluated for continuous spray evaluation as per USP, drug content, spray angel, spray pattern, ex vivo release study, skin irritation study, stability study etc.
Compatibility of aerosol was evaluated using glass container. Product concentrate and propellant (LPG) was found to be compatible. Particles size of Tazarotene topical spray was determined by using microscopic method. Particles sizes of topical aerosol are usually less than 100 µm. Particles size is influenced by many factors. Among them are vapour pressure, the type and amount of solvents present in the formula, the type and amount of the propellant used, and the design of the valve system. Particle size also gives the information about stability of topical spray.
Delivery rate and delivery amount was found to be same and affected by vapour pressure. Net content of topical spray was within labeled amount. No leakage was detected when containers were passed through filled water bath at 55°C. pH of topical spray indicated that Tazarotene topical spray was suitable for topical application without producing any irritation.
Tazarotene topical spray was found to be flammable due to present of solvent and LPG (propellant). Spray pattern of selected formulation was revealed the similarity with almost same diameter for all formulation.
Skin irritation studies showed that no erythema or edema was found to occur on rats at the end of 24hrs. Thus, optimized formulations can be considered as safe and non-irritant for topical application.
Stability study data for 20 days at 40°C±2°C temperature and 75%RH±5%RH revealed that product was found to be stable. The results showed that when LPG and aluminium were used as the propellant and the container respectively, they produced Tazarotene topical spray having the desired characteristics and no interaction was found between aerosol concentrate and canister.
Hence, topical spray of Tazarotene would have to be a better alternative as a topical drug delivery system for treatment of acne.
From the obtained values in the present work, it can be concluded that the Topical spray formulations for Tazarotene can be an innovative and promising approach for the topical administration of Tazarotene.
Such a topical delivery formulation will have better patient compliance and acceptability.

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