CLINICAL STUDY REPORT

Human Skin Patch Test

EVALUATION OF DERMATOLOGICAL SAFETY OF INVESTIGATIONAL PRODUCT BY HUMAN SKIN IRRITATION TEST ON HEALTHY HUMAN VOLUNTEERS AS PER IS 4011:2018

PROTOCOL NO: ACS/PT/01/2024

Investigational Product	**Auretics BP Management Spray**
Batch/ Product code	-
Product Form	Liquid
Sponsor	**Auretics Limited** Plot No. 190, Old Block Near LIC Colony, Mangal Bazar Road, Dilshad Garden, Delhi – 110095
CRO Address	**Amruth Biological and Clinical Service Private Limited** #78, 9th Cross, 1st N Block, Rajajinagar, Bengaluru 560 010, India
Study Summary	The study is conducted in 24 human volunteers for duration of 7 days. Product was evaluated through single application of closed patch test under occlusion for 24 hrs. After patch removal, skin was observed for irritation reactions at 0 hr, 24hr, 48hrs post patch removal for immediate reactions and 7 days post patch removal for delayed reactions.
Study Conclusion	The **test product** emerged as **non-irritant** when observed at 0hr, 24 hours, 48 hours and 7 days post patch removal. Positive control was confirmed as mild-irritant when observed at 0hr, 24 hrs, 48 hrs and non-irritant at 7 days of post patch removal. Negative control was confirmed as non-irritant when observed at 0hr, 24 hours, 48 hours and 7 days post patch removal. The study concludes that **the test product (Auretics BP Management Spray) passes the skin irritation test and found to be non-irritant.**

TRIAL SUMMARY

Protocol Title	Evaluation of dermatological safety of investigational product by human skin irritation test on healthy human volunteers as per IS 4011:2018
Principal Investigator	**Dr. Sunil Kumar S** MBBS, MD (Dermatology), MBBS, MD, Dermatologist, Cosmetologist and Hair Transplantation Surgeon, Professor in Dermatology, AIMS & RC, Bengaluru
Sponsor	**Arjun Gupta** C/o Auretics Limited Plot No. 190, Old Block Near LIC Colony, Mangal Bazar Road, Dilshad Garden, Delhi – 110095
Study Site	**Sree Maruti Hospital** No. 67, Link Road, Sheshadripuram, Bengaluru 560020
Study duration	9 days
Study commencement date	02/04/2025
Study completion date	10/04/2025
Date of report issue	21/04/2025
Investigational Product	**Auretics BP Management Spray**
Positive Control	1% Sodium Lauryl Sulphate in distilled water
Negative Control	0.9% Isotonic Saline solution
Study schedule	Date of patch application:- 02/04/2025 Date of observation 0 hrs post patch removal :- 03/04/2025 Date of observation 24 hrs post patch removal :- 04/04/2025 Date of observation 48 hrs post patch removal: - 05/04/2025 Date of observation 7 days post patch removal :- 10/04/2025

INVESTIGATOR'S DECLARATION:

I, the undersigned have read this clinical study report and hereby confirm that the study was conducted in accordance with Ethics Committee approved protocol and also with all the applicable regulatory requirements regarding the obligations of the Investigator and all other pertinent requirements of the ICH Guidelines for Good Clinical Practice. I further agree and confirm that all associates involved in the study were informed and aware of their study obligations and completion.

Protocol Number: ACS/PT/01/2025

Title: Evaluation of dermatological safety of investigational product by human skin irritation test on healthy human volunteers as per IS 4011:2018.

Dr. Sunil Kumar S MBBS MD
Dermatologist
KMC NO. 72239

21/04/2025

SIGNATURE OF THE PRINCIPAL INVESTIGATOR DATE

Name of the Principal Investigator: Dr. Sunil Kumar S, MBBS, MD, Dermatologist, Cosmetologist and Hair Transplantation Surgeon,
Professor in Dermatology, AIMS & RC, Bengaluru
Sree Maruti Hospital
No. 67, Link Road, Sheshadripuram, Bengaluru 560020

1. STUDY SYNOPSIS:

Study title	Evaluation of dermatological safety of investigational product by human skin irritation test on healthy human volunteers as per IS 4011:2018.
Clinical phase	Early Phase safety study – Patch tests
Study duration	9 days
Study objectives	To evaluate the safety of cosmetic products
Study design	Open label, Safety study
Number of volunteers to be enrolled	24 subjects
Inclusion Criteria	1) Voluntary men/women between 18 and 65 years. 2) Photo type III to V. 3) Having apparently healthy skin on test area. 4) For whom the investigator considers that the compliance will be correct. 5) Cooperating, informed of the need and duration of the examinations and ready to comply with protocol procedures. 6) Having signed a Consent Form. 7) Willingness to avoid intense UV exposure on test site (sun or artificial UV), during the course of the study. 8) Willingness to avoid excessive water contact (for example swimming) or activity which causes excessive sweating (that is exercise, sauna…), during the course of the study. 9) Should be able to read and write (in English, Hindi or local language). 10) Having valid proof of identity and age.
Exclusion criteria	1) Pregnant/nursing mothers 2) Scars, excessive terminal hair or tattoo on the studied area. 3) Dermatological infection/pathology on the level of studied area.

	4) Hypersensitivity, allergy antecedent (to any cosmetic product, raw material or hair dye). 5) Any clinically significant systemic or cutaneous disease, which may interfere with study treatment or procedures. 6) Chronic illness which may influence the outcome of the study. 7) Subjects on any medical treatment either systemic or topical which may interfere with the performance of the study treatment (presently or in the past 1 month). 8) Subject in an exclusion period or participating in another food, cosmetic or therapeutic trial.
Control product	1) Positive control (1% w/v Sodium Lauryl Sulphate) 2) Negative control (0.9% of Isotonic Saline solution)
Study schedule	Visit 1 (Day of Screening and patch application) Visit 2 (Day of patch removal and observation: 0hr post patch removal) Visit 3 (Day of observation: 24hr post patch removal) Visit 4 (Day of observation: 48hr post patch removal) Visit 5 (Day of observation: 7th day post patch removal)
Primary end point	To assess the Safety of the Investigational product (IP)
Safety analysis	This evaluation will summarize the recorded adverse events, clinical parameter assessment with erythema scale.
Statistical methods	Vitals and Demographic characteristics and result of the study will be summarized with the descriptive statistics including mean and Standard deviation and frequency percentages will be evaluated for safety parameters. AE will be summarized with a number and the percentage.

2. STATEMENT OF COMPLIANCE

Ethics: Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

Trial risk vs trial benefit: Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.

Trial participants: The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

Information on the Medicinal Product: The available non-clinical and clinical information on an Investigational Product should be adequate to support the proposed clinical trial.

Good quality trials: Clinical trials should be scientifically sound, and described in a clear, detailed protocol.

Compliance with the study protocol: A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.

Medical decisions: The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

Trial staff: Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).

Informed consent: Freely given informed consent should be obtained from every subject prior to clinical trial participation.

Clinical trial data: All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

Confidentiality: The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

Good Manufacturing Practice: Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

Quality assurance: Systems with procedures that assure the quality of every aspect of the trial should be implemented.

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3. ETHICS COMMITTEE:

3.1 Institutional Review Board:

All the study related documents were reviewed by **Institutional Ethics Committee, Bangalore Ethics committee, Sri Venkateshwara Hospital Ethics Committee, Sarjapur**, Attibele Main Road, Bangalore 562107, Karnataka, India prior to study initiation. The study was conducted in compliance with Part 56 of Title 21 of the Code of Federal Regulations (CFR) and International Conference on Harmonization (ICH) guidelines. The aforementioned Ethics Committee was registered under DCGI vide registration number **ECR/298/Inst/KA/2013/RR-19.**

3.2 Ethical Conduct of the Study:

This research was conducted in accordance with the clinical research guidelines established by the Supplements and Cosmetics Act, 1940 of India, Supplements and Cosmetics Rules, 1945 of India, Ethical Guidelines for Biomedical Research on Human Participants, 2006 of Indian Council of Medical Research (ICMR) in India, the principles enunciated in the Declaration of Helsinki (Edinburgh, 2000) and the ICH-harmonized tripartite guideline regarding Good Clinical Practice (GCP). Written and oral information about the study in a language understandable by the subject was provided to all subjects. Each subject was informed by the investigator, prior to the screening evaluation, of the purpose of this clinical trial, including possible risks and benefits and documented the informed consent process in the subject's chart. Prior to entry into the study or initiation of any study-related procedures, the subject read, signed and dated the IEC approved informed consent form. Sufficient time was provided for each subject to decide whether to participate in the study and all the questions and clarifications regarding the study were clarified by the investigator. The original signed informed consent form has been retained by the study site and a copy was given to the subject. The form summarized, in non-technical terms, the purpose of the study, the procedures to be carried out, and the potential hazards.

4. INTRODUCTION:

Irritants are substances that may damage the skin. The damage will depend upon the nature, concentration and duration of exposure. Irritation is manifested as erythema (redness), edema (swelling), vesiculation and finally to an intense suppurate reaction without the involvement of

immune system. The irritation potential of a substance can be assessed in human patch test. This patch test was carried out on human volunteers, only after ensuring that all the ingredients used have acceptable toxicological end points based on available literature or by carrying out alternate evaluation techniques. No product with unknown ingredient should be directly tested in humans. The same is also applicable for new/novel ingredients.

4.1 Test Procedure:

The neat cosmetic product was first applied on the upper arms or back of human subjects. The skin essentially seen carefully to be non-hairy and free from any type of skin lesions or other dermatological problems. In case of the hairy back, the hair was cut off by clipper or shaver before applying the patches, and care was taken to avoid any abrasions, cuts or lesions. In case of rinse off products, rinsed the treated sites with water to remove any leftover residue after removal of the patch (or the specified time of contact in case of open patch). If the volunteer experienced unbearable discomfort with any of the patches the volunteer was instructed to remove such patches any time prior to the targeted 24 h contact (where applicable). Such sites were marked with a blue/ black skin marker to facilitate evaluation later. The volunteer was also requested to note down the sign and symptoms of the discomfort and the time of removal of the patch and hand it over to the investigator. The skin reactions were assessed subjectively using the Draize scale, 24 h after removal of the patches. Followed up the reactions if any, after one week to confirm recovery and later if necessary at the discretion of the investigator.

4.2 Test patches for topical treatment:

The ready-made standard test patches (Finn chambers/IQ chambers or such suitable equivalent) measuring about 1 cm diameter or 1 sq cm was used. 0.04 mg of the sample was taken using a micropipette or weighing balance (as applicable) on the patch. Then the patch applied on the upper arm or back.

4.3 Patch loading method:

40 µg/µl of investigational product (without dilution) was applied on the precut filter paper placed inside the allotted Derma proof Aluminium Finn chamber prefixed to a scanpore tape. Patch was applied on upper arm or back.

40µl of positive control (Sodium Lauryl Sulphate, diluted to a concentration of 1% w/v) and 40µl of negative control (0.9% Isotonic Saline solution) was pipetted out on allotted Derma proof Aluminium Finn chamber prefixed to a scanpore tape.

4.4 Scoring method:

Scoring of irritation is as per the clause 4.3.1.3 on Draize scale for scoring treatment sites. IS 4011:2018, no reaffirmed, third revision (ICS 71.100.40), (Clauses 4.3.1.3 and 4.3.2.6) BIS 2018.

Draize Scale for Irritation Score

Score For Erythema	Reaction	Score For Oedema	Reaction
0	No reaction	0	No Oedema
1	Very slight erythema/dryness with shiny appearance	1	Very slight Oedema
2	Slight erythema/ dryness /wrinkles	2	Slight Oedema
3	Moderate erythema/ dryness /wrinkles	3	Moderate Oedema
4	Severe erythema/ wrinkles/scales	4	Severe Oedema

Mean Score for Irritation = $\frac{\text{Total score (Erythema + Oedema) for each sample}}{\text{Total no. of Subject}}$

Assessment of mean scores:

Mean Score	Classification
0.0 to 2.0	Non Irritant
Up to 2.0 to 4.0	Mild Irritant
Above 4.0 to 8.0	Irritant

4.5 Dermatologist's visual assessment:

Test sites were assessed for erythema / dryness/ wrinkles and oedema as per the Draize scale for scoring at the treatment site.

4.6 Subject's visual assessment:

Subjects' feedback on skin irritation sensations such as burning, itching, stinging and tingling was recorded at baseline, 0hr, 24 hrs, 48 hrs and 7 days post patch removal.

Individual subject's irritation assessment scores by Dermatologist are tabulated in separate tables under the result section.

4.7 Materials for patch preparation:

- Derma proof Aluminium Finn chamber prefixed to a scanpore tape
- Investigational Product, Positive control and Negative control
- Microbalance or Micropipette
- Appropriately cut filter paper

5. DESCRIPTION OF INVESTIGATIONAL PRODUCTS:

Investigational Product	**Auretics BP Management Spray**
Product Form	**Liquid**
Batch Number	**A411**
Sponsor detail	**Arjun Gupta** C/o Auretics Limited Plot No. 190, Old Block Near LIC Colony, Mangal Bazar Road, Dilshad Garden, Delhi – 110095

5.1 Investigational Products Supply, Labeling, Dispensing and Accountability Procedures:

- The Sponsor supplied sufficient quantities of the IPs (Investigational Products) for the study conduct, properly labeled according to the requirements of GMP.

- It was the responsibility of the Sponsor to ensure that appropriate Investigational Product identification, assay testing and dissolution profiles for all the test and reference products are provided to clinical study center before starting the study.
- The Investigational Products were received by the Principal Investigator or Clinical Investigator or Research Pharmacist or a suitable designate from the concerned department along with Certificate of Analysis (COA) with dissolution tests.
- IPs was supplied in an appropriate package deemed to maintain the integrity of the products.
- Records were made of the receipt and dispensing of clinical supplies to provide complete accountability of all supplies.
- The supplies were stored at controlled temperature as per label instructions or as per COA in pharmacy accessible only to the pharmacist or authorized personnel.
- Batch number/lot number, manufacturing date, manufactured by and expiry date for all IPs were included in the final report.
- Under the supervision of Investigator & QA personnel, the designated pharmacist dispensed the study product.
- Study products were dispensed as an additional, in order to handle any unexpected loss or damage of the investigational product during administration process.
- Records were made of the receipt and dispensing of clinical supplies to provide a complete accountability of all supplies.

5.2 Labeling of Investigational Product:

The following information was given on the dosing label prepared for the study;

"For Clinical Studies only"

- Batch No.
- Dose & Dosage form
- Manufactured by and address
- Manufacturing date
- Expiry date
- Indication

5.3 Test Product Description:

IP No.	Product	Product Type	Batch/ Product code	Manufactured by
1.	Auretics BP Management Spray	Liquid	A411	**Auretics Limited** A-10/15, Jhilmil Industrial Area, Delhi – 110095
2.	Positive Control (1% SLS)	Solid	F2OA/0120/0106/21	**SD Fine Chem limited** 1502, MarathonIcon, Lower Parel, Mumbai - 400013
3.	Negative Control (0.9% normal saline)	Liquid	2242221	**Otsuka pharmaceutical India Private Limited** Village – Vasana – Chacharwadi, Taluka- Sanand, Ahmedabad, Gujarat 382213

5.4 Dilution Method:

S.No	Sample	Product Type	Dilution
1.	Auretics BP Management Spray	Liquid	No dilution
2.	Positive Control (1% SLS)	Solid	1% w/v (0.25g of Sodium Lauryl Sulphate in 25 ml of distilled water)
3.	Negative Control (0.9% normal saline)	Liquid	No dilution

6. STUDY OBJECTIVE:

6.1 Overall Purpose of the Study:

To evaluate the dermatological safety of the investigational product on healthy human subjects.

6.2 Primary Objective:

To assess the Dermatological Safety of the Investigational product.

7. INVESTIGATIONAL PLAN:

7.1 Study Design:

A prospective, open-label, Safety study.

7.2 Subject Sample Size:

24 subjects

7.3 Randomization:

Not applicable.

7.4 Study Product Administration:

- Topical application

7.5 Overall Trial Design:

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
Screening/ Visit 1	Visit 2	Visit 3	Visit 4	-	-	-	-	Visit 5
Patch Application	0 hr Observation	24 hr Observation	48 hr Observation	-	-	-	-	7th day Observation

7.6 Subject Selection Criteria:

The following criteria were verified after obtaining a written and signed informed consent form from the subject or their caretaker or legally acceptable representative. Records of all subjects if included or excluded after an informed consent process were maintained on the study records with reasons for exclusion or withdrawal from the study. Subject Identifiers (ID) were given only to eligible subjects per the assignment instructions.

7.6.1 Inclusion Criteria:

- Voluntary men/women between 18 and 65 years.
- Photo type III to V.
- Having apparently healthy skin on test area.
- For whom the investigator considers that the compliance will be correct.
- Cooperating, informed of the need and duration of the examinations and ready to comply with protocol procedures.
- Having signed a Consent Form.
- Willingness to avoid intense UV exposure on test site (sun or artificial UV), during the course of the study.
- Willingness to avoid excessive water contact (for example swimming) or activity which causes excessive sweating (that is exercise, sauna…), during the course of the study.
- Should be able to read and write (in English, Hindi or local language).
- Having valid proof of identity and age.

7.6.2 Exclusion Criteria:

- Pregnant/nursing mothers
- Scars, excessive terminal hair or tattoo on the studied area.
- Henna tattoo anywhere on the body (in case of studies involving hair dyes).
- Dermatological infection/pathology on the level of studied area.
- Hypersensitivity, allergy antecedent (to any cosmetic product, raw material or hair dye).
- Any clinically significant systemic or cutaneous disease, which may interfere with study treatment or procedures.
- Chronic illness which may influence the outcome of the study.
- Subjects on any medical treatment either systemic or topical which may interfere with the performance of the study treatment (presently or in the past 1 month).
- Subject in an exclusion period or participating in another food, cosmetic or therapeutic trial.

7.7 Treatment Procedure / Schedule of Events:

S. No.	Parameters	Screening/ Visit 1	0 hr/ Visit 2	24 hr/ Visit 3	48 hr/ Visit 4	7th day/ Visit 5
1.	Briefing subjects for study / ICF	X	-	-	-	-
2.	Demographics and Vitals	X	-	-	-	-
3.	Medical History	X	-	-	-	-
4.	General Physical examination	X	-	-	-	-
5.	Dermatological examination	X	-	-	-	-
6.	Inclusion criteria/Exclusion	X	-	-	-	-
7.	Concomitant Medications	X	X	X	X	X
8.	Dermatological Assessment	X	X	X	X	X
9.	Patch Application	X	-	-	-	-
10.	Patch Removal	-	X	-	-	-
11.	Adverse Event/ Serious Adverse Event Monitoring	-	X	X	X	X

7.8 Screen Failures:

Subjects who screened and found to be unsuitable for the study as determined by medical examination, physical examination was recorded citing reasons for their rejection and they were followed up, counseled if necessary.

7.9 Withdrawal Criteria:

A subject may voluntarily discontinue study participation at any time. The investigator may also discontinue the subjects study participation at any time at his/her discretion. The circumstance applicable for the subjects to discontinue from the study were following;

- Withdrawal of consent by the subject to continue in the study.
- Development of a serious or intolerable adverse event which necessitate discontinuation as the discretion of the Investigator.
- At the initiation of the Investigator, in the situation where the subject does not adhere to the study procedures.
- Protocol deviation/violation occurs that in the opinion of sponsor warrants discontinuation

from study.

- Subject experiences an allergic reaction / anaphylaxis to investigational product.

7.10 Concomitant medication:

Details of con-med including but not limited to name, indication, dosages, and start/stop time periods, will be captured in the con-med forms of the respective subject.

7.11 Study Safety and Efficacy Assessment:

Safety parameters for this study will include the vitals, adverse events and will be compared from baseline to final visit of the subjects. A physician will do medical examination of the subjects at admission and prior to discharge. Wellbeing assessment of subjects is done at all sessions of vitals measurements and medical examination. Any abnormal results which are clinically significant as judged by the investigator will be considered as adverse events and necessary treatment and follow-up shall be given.

7.12 Quality Control and Quality Assurance:

- The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).
- The sponsor is responsible for securing agreement from all involved parties to ensure direct access to all trial-related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.
- Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.
- Agreements, made by the sponsor with the investigator/institution and any other parties involved with the clinical trial, should be in writing, as part of the protocol or in a separate agreement.

7.13 Statistical Considerations:

Vitals and Demographic characteristics and result of the study will be summarized with the descriptive statistics including average and Standard deviation and frequency percentages will be evaluated for safety parameters. AE will be summarized with a number and the percentage.

8. TRIAL SUBJECTS:

Subject Code	Screened	Randomized	Dropouts	Discontinued	AE/SAE
001	Yes	NA	No	No	No
002	Yes	NA	No	No	No
003	Yes	NA	No	No	No
004	Yes	NA	No	No	No
005	Yes	NA	No	No	No
006	Yes	NA	No	No	No
007	Yes	NA	No	No	No
008	Yes	NA	No	No	No
009	Yes	NA	No	No	No
010	Yes	NA	No	No	No
011	Yes	NA	No	No	No
012	Yes	NA	No	No	No
013	Yes	NA	No	No	No
014	Yes	NA	No	No	No
015	Yes	NA	No	No	No
016	Yes	NA	No	No	No
017	Yes	NA	No	No	No
018	Yes	NA	No	No	No
019	Yes	NA	No	No	No
020	Yes	NA	No	No	No
021	Yes	NA	No	No	No
022	Yes	NA	No	No	No
023	Yes	NA	No	No	No
024	Yes	NA	No	No	No

9. SAFETY EVALUATION:

9.1 Adverse Event Monitoring:

- The clinical investigator or a medical officer will be available within the clinical facility until 24 hrs post dose during each period. Medically qualified personnel or any specialist will be also available on call until the completion of the study. Subjects will be monitored throughout the study period for adverse events.
- Subjects will be informed to bring to the notice of the doctor or nurse or any other staff any adverse event that may occur during their Study period. Treatment of the adverse events will be done by a physician, either with in the clinical facility or at a nearby hospital.
- All the adverse events will be recorded and reported as per relevant SOP and will be followed until their resolution.

9.2 Intensity of Adverse Events:

***Mild*:** events require minimal or no treatment and do not interfere with the subject's daily activities.

Moderate: events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.

Severe: events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually incapacitating.

Life threatening: any adverse drug experience that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that had it occurred in a more severe form, might have caused death. Changes in the severity of an AE should be documented to allow an assessment of the duration of the event at each level of intensity to be performed. Adverse events characterized as intermittent require documentation of onset and duration of each episode.

9.3 Serious Adverse Events:

Investigator(s) will report all serious and unexpected adverse events to the Licensing Authority, to the Sponsor and the Ethics Committee within twenty-four hours of their occurrence.

Serious Adverse Event (SAE): An SAE is defined as an AE that meets one of the following conditions:

- Death during the period of protocol defined surveillance Life-threatening event (defined as a subject at immediate risk of death at the time of the event)
- An event requiring inpatient hospitalization or prolongation of existing hospitalization during the period of protocol defined surveillance
- Results in congenital anomaly or birth defect
- Results in a persistent or significant disability/incapacity

Any other important medical event that may not result in death, be life threatening, or require hospitalization, may be considered a serious adverse experience. All SAEs (if any) had been recorded on the appropriate CRF and SAE form followed through resolution by a study clinician reviewed and evaluated by a study clinician.

9.4 Reporting Procedures for AE and SAE:

9.4.1 for AE:

- Through telephone contacts and subject visits to the study site, the Investigator and/or designee will inquire about adverse experiences and document the inquiry in the subject's medical chart.
- During visits to the site, the Monitor will ensure that if an adverse experience is found, the Study Coordinator documents the following in the subject's Case Report Form:
- Date and time (if applicable) the event started and ended.
- Description to the event.
- Severity and Outcome of the event.
- Action taken and Relationship to study supplement

9.4.2 for SAE:

Any AE considered serious by the PI or Sub investigator or which meets the aforementioned criteria must be submitted on an SAE form to the Sponsor.

9.5 Obligation of the sponsor:

During the course of the study, the Sponsor will report in an expedited manner all SAEs that are both unexpected and at least reasonably related to the IP, to the Authorities, IECs / IRBs as appropriate and to the Investigators. In addition, the Sponsor may report in an expedited manner all SAEs that are expected and at least reasonably related to the IPs to the Authorities, according to local regulations.

9.6 Follow up of subjects after Adverse Events:

- The Investigator due responsibility was to follow up and take all appropriate measures to ensure the safety of the patients, notably he/she was responsible to follow up the outcome of any Adverse Events until the return to normal condition.
- In case of any Serious Adverse Event, the Investigator was responsible be followed up to the patient until clinical recovery is completed and have returned to normal, or until progression has been stabilized.
- This also implied that follow-up will be continue after the patient has left the Clinical Trial and that additional investigations may be requested by the Monitoring Team.

10. RESULTS:

Table 1: Baseline Characteristics

Age	
Number of Subject	**24**
Mean	**38.38**
Median	**40.50**
Minimum	**23.00**
Maximum	**60.00**

Gender	Frequency	Percent
Male	7	23.3
Female	17	56.7
Total	24	100

Table 2: Vitals

Parameter	Normal	Abnormal
Temperature, n[%]	24 (100.0)	0 (0.0)
Heart Rate, n[%]	24 (100.0)	0 (0.0)
Pulse Rate, n[%]	24 (100.0)	0 (0.0)
Respiratory Rate, n[%]	24 (100.0)	0 (0.0)
Systolic Blood Pressure, n[%]	24 (100.0)	0 (0.0)
Diastolic Blood Pressure, n[%]	24 (100.0)	0 (0.0)

Table 3: Physical Examination

Parameter	Normal	Abnormal
General Appearance, n[%]	24 (100.0)	0 (0.0)
Head, Ears, Nose, and Throat, n[%]	24 (100.0)	0 (0.0)
Heart, n[%]	24 (100.0)	0 (0.0)
Lungs, n[%]	24 (100.0)	0 (0.0)
Abdomen, n[%]	24 (100.0)	0 (0.0)
Extremities, n[%]	24 (100.0)	0 (0.0)
Neurological, n[%]	24 (100.0)	0 (0.0)

Table 4: Medical History

Parameter	Yes	No
Head, Ears, Nose, Throat, n[%]	0 (0.0)	24 (100.0)
Cardiovascular, n[%]	0 (0.0)	24 (100.0)

Parameter	Yes	No
Respiratory, n[%]	0 (0.0)	24 (100.0)
Endocrine, n[%]	0 (0.0)	24 (100.0)
Gastrointestinal, n[%]	0 (0.0)	24 (100.0)
Hepatobiliary, n[%]	0 (0.0)	24 (100.0)
Genitourinary, n[%]	0 (0.0)	24 (100.0)
Musculoskeletal, n[%]	0 (0.0)	24 (100.0)
Neurological, n[%]	0 (0.0)	24 (100.0)
Psychological, n[%]	0 (0.0)	24 (100.0)
Hematological, n[%]	0 (0.0)	24 (100.0)
Immunological, n[%]	0 (0.0)	24 (100.0)
Dermatological, n[%]	0 (0.0)	24 (100.0)
Allergies, n[%]	0 (0.0)	24 (100.0)
Other, n[%]	0 (0.0)	24 (100.0)

Table 5: Inclusion and Exclusion Criteria

Parameter	Yes	No
Inclusion Criteria, n[%]	24 (100.0)	0 (0.0)
Exclusion Criteria, n[%]	0 (0.0)	24 (100.0)

Table 6: Concomitant Medication

Parameter	Yes	No
Concomitant Medication, n[%]	0 (0.0)	24 (100.0)

Table 7: Dermatological assessment scores for skin erythema, oedema and mean irritation scores for Investigational Product – Auretics BP Management Spray

Subject Number	0hr post Patch removal		24hr post patch removal		48hr post patch removal		7 days post patch removal	
	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema

1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0

Mean irritation score	**0hr post patch removal**	**24hr post patch removal**	**48hr post patch removal**	**7 days post patch removal**
	0.00	0.00	0.00	0.00

Observation: The test product mentioned above in the document emerged as non- irritant product when observed at 0hr, 24 hrs, 48 hrs and 7th day of post patch removal.

Table 8: Dermatological assessment scores for skin erythema, oedema and mean irritation scores for Positive control - 1% Sodium Lauryl Sulphate.

Subject Numbe	**0hr post patch removal**		**24hr post patch removal**		**48hr post patch removal**		**7 days post patch removal**	
	Erythe	**Oedem**	**Erythem**	**Oedem**	**Erythem**	**Oedem**	**Erythem**	**Oedem**
1	2	2	1	1	1	1	0	0
2	2	1	2	1	1	1	0	0

3	2	1	2	1	2	1	0	0
4	2	2	2	1	1	1	0	0
5	2	2	1	1	1	0	0	0
6	3	2	2	1	2	1	0	0
7	2	1	2	1	2	1	0	0
8	2	2	1	1	1	1	0	0
9	2	2	1	1	1	1	0	0
10	2	1	1	1	1	0	0	0
11	2	2	1	1	1	1	0	0
12	2	2	2	1	2	1	0	0
13	2	1	2	1	2	1	0	0
14	2	1	2	1	1	1	0	0
15	2	2	1	1	1	1	0	0
16	2	1	1	1	1	0	0	0
17	2	1	1	1	1	1	0	0
18	2	1	1	1	1	1	0	0
19	2	1	1	1	1	1	0	0
20	2	1	1	1	1	0	0	0
21	2	2	2	1	1	1	0	0
22	2	1	2	1	1	1	0	0
23	2	1	1	1	1	0	0	0
24	2	1	2	1	2	1	0	0

Mean irritation score	**0hr post patch removal**	**24hr post patch removal**	**48hr post patch removal**	**7 days post patch removal**
	3.45	2.45	2.04	0.00

Observation: Positive control - **1% Sodium Lauryl Sulphate** was confirmed as mild-irritant at 0hr, 24 hrs, 48 hrs and non-irritant at 7th day of post patch removal.

Table 9: Dermatological assessment scores for skin erythema, oedema and mean irritation scores for Negative control – 0.9% Isotonic Saline solution

Subject Number	**0hr post patch removal**		**24hr post patch removal**		**48hr post patch removal**		**7 days post patch removal**	
	Erythema	**Oedema**	**Erythema**	**Oedema**	**Erythema**	**Oedema**	**Erythema**	**Oedema**
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0

4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0

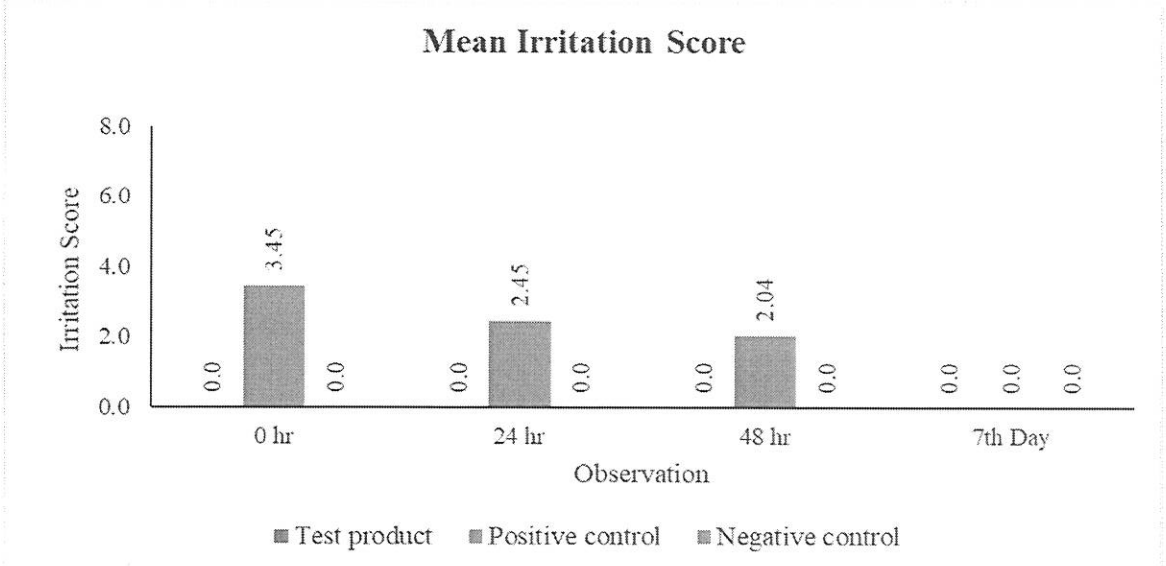
Mean irritation score	**0hr post patch removal**	**24hr post patch removal**	**48hr post patch removal**	**7 days post patch removal**
	0.00	0.00	0.00	0.00

Observation: Negative control - 0.9% Isotonic Saline solution was emerged as non-irritant when observed at 0hr, 24 hrs, 48 hrs and 7th day of post patch removal.

Table 10: Average mean skin irritation score for each tested formulation:

Investigational Product	Mean Irritation Score – 0 hr	Irritancy assessment	Mean Irritation Score – 24 hrs	Irritancy assessment	Mean irritation Score- 48 hrs	Irritancy assessment	Mean Irritation Score – 7th day	Irritancy assessment
Auretics BP Management Spray	0.00	Non Irritant	0.00	Non Irritant	0.00	Non Irritant	0.00	Non Irritant
Positive control (1%SLS)	3.45	Mild Irritant	2.45	Mild Irritant	2.04	Mild Irritant	0.00	Non Irritant
Negative control (0.9% NS)	0.00	Non Irritant	0.00	Non Irritant	0.00	Non Irritant	0.00	Non Irritant

Graph 1: Mean Irritation Score



11. DISCUSSIONS:

Irritants are substances that may damage the skin. The damage will depend upon the nature, concentration and duration of exposure. Irritation manifested as erythema (redness), edema (swelling), vesiculation and finally to an intense suppurate reaction without the involvement of immune system. The irritation potential of a substance can be assessed in human patch test. This patch test was carried out on human volunteers, only after ensuring that all the ingredients used have acceptable toxicological end points based on available literature or by carrying out alternate evaluation techniques. No product with unknown ingredient had been directly tested in humans. The same is also applicable for new/novel ingredients.

The trial was conducted in Sree Maruti Hospital No. 67, Link Road, Sheshadripuram, Bengaluru 560020with Dr. Sunil Kumar S as Principal investigator, post Independent Ethics Committee approval /favorable opinion on the trial proposal.

Eligible subjects were enrolled into the study only after obtaining their Informed Consent Form. Total 24 subjects aged 18-65 years were enrolled in the study as per the study protocol procedures. Subject's Age, Sex, Height, Weight, BMI and other Vitals were measured and the subjects were followed up with monitoring visits, safety assessments and concomitant medications.

Baseline Characteristics and Vitals: Baseline Characteristics (Table 1) – Age and Gender, Vitals were completely assessed in all the subjects. Vitals (Table 2) parameters like Temperature, Heart rate, Pulse rate, Respiratory rate, Systolic and Diastolic blood pressure were found to be normal for all the study subjects.

Safety Parameters: Physical Examination (Table 3) like General Appearance, ENT, Heart, Lungs, Abdomen, Extremities, Neurological parameters were found to be normal for all the study subjects. Medical history (Table 4) like ENT, Cardiovascular, Respiratory, Endocrine, Gastrointestinal, Hepatobiliary, Genitourinary, Musculoskeletal, Neurological, Psychological, Hematological, Immunological, Dermatological, Allergies and other conditions were not seen any study subjects. Based on (Table 5) Inclusion and Exclusion Criteria, study subjects are enrolled in the study. Concomitant Medication (Table 6) shows that no subjects undergone for any other medications during their study period.

Safety Assessments: (Table 7) Dermatological assessment scores for skin erythema, oedema and mean irritation scores for Investigational Product, (Table 8) Dermatological assessment scores for skin erythema, oedema and mean irritation scores for Positive control - 1% Sodium Lauryl Sulphate, (Table 9) Dermatological assessment scores for skin erythema, oedema and mean irritation scores for Negative control – 0.9% Isotonic Saline solution. (Table 10) Average mean skin irritation score for each tested formulation. (Graph 1) Mean Irritation Score.

There were no Adverse Event/Serious Adverse Events reported during the entire study duration. There were no protocol deviations observed during the course of the study. There were no dropouts and subject discontinuation in the study.

12. CONCLUSION:

As per Draize scale for scoring and its interpretation to classify the Products based on its irritancy potential with mean score obtained from the study subjects based on the reaction of test product and control product. The test product emerged as non-irritant when observed at 0 hour, 24 hours, 48 hours and 7 days of post patch removal. Positive control was confirmed as mild-irritant when observed at 0 hour, 24 hours, 48 hours and non-irritant at 7 days of post patch removal. Negative control was confirmed as non-irritant when observed at 0 hour, 24 hours, 48 hours and 7 days of post patch removal. Hence the study concludes that the **test product - Auretics BP Management Spray proven as non-irritant** and suitable for all skin types under Fitzpatrick scale III to V from Medium white to Brown or Dark brown skin.

13. REFERENCES :

1. *Study method is based on the Bureau of Indian Standards (BIS) method 4011:2018 Amendment-1 (July 2018).*

2. *Test method described in IS 4011:2018 Methods of test for safety evaluation of cosmetics, no reaffirmed, third revision (ICS 71.100.40), (Clauses 4.3.1.3 and 4.3.2.6) BIS 2018. Irritation scoring system is as per the clause 4.3.1.3, 4.3.1.2 on Draize scale for scoring treatment sites.*