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Development and Evaluation of Punica Granatum Peel Gel as a Potential Anti-Ulcer Agent

FORMULATION AND EVALUATION OF HERBAL GEL OF PUNICAGRANATUM PEEL

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Abstract: The herbal gel was prepared by using different concentrations of extract of pomegranate peel powder and Carbopol 934, Propylene paraben as a gel base and other ingredients like Tulsi leaves extract, propyl paraben, propylene glycol, triethanolamine, lemon essential oil, etc.

Formulations were evaluated for various parameters. The formulated gel was transparent, homogeneous and pH ranged from 5.5 to 6.8. The formulation showed acceptable rheological behavior with applicable spreadability and extrudability properties. Herbal medicine is still the mainstay of about 75-80% of the world's population, mainly in developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effect from the experimental evidence of invitro studies it was observed that extract of pomegranate peel powder contain tannin so it showed significant anti-inflammatory and antioxidant effect.

Developed herbal formulation was stable, safe and effective over to synthetic formulations for the treatment of mouth ulcer. There are number of synthetic gels in the market as compare to herbal or natural gel, synthetic gel has harmful effect on skin like skin irritation and dryness of skin.

***IndexTerms* - Pomegranate, Tulsi, Mouth ulcer gel, Herbal gel.**

INTRODUCTION:

Gel is the most common form of ulcer treatment gels are primarily been products aimed at curing the mouth ulcer. In the present scenario, it seems improbable that herbal gel, although better in performance and safer than the synthetic ones, will be popular with the consumers. A more radical approach in popularizing herbal gel would be to change the consumers' expectations from a gel, with emphasis on safety and efficacy. The present paper emphasizes on composition, formulation, methods of evaluation of herbal mouth ulcer gel.

Gels are typically semi-solid formulations having a liquid phase that has been thickened with other components. Uses of topical gel preparations are for skin application or percutaneous penetration of medicament or local action to certain mucosal surfaces. A mouth ulcer is a break or breach in the mucous membrane, which is lines the inside of the mouth. It usually has yellow or white color and usually looks like a depression in the mouth that is the mucous membrane. The Commercially available gels contain synthetic and semi-synthetic active agents which have several disadvantages like staining on the teeth, irritation, and burning sensation only because presence of high degree of alcohol content and some organic compounds. The present investigation deals with use of herbal powdered Tulsi and pomegranate in the treatment of mouth ulcer in the pharmaceutical gel.

Ulcers are recurrent lesions that result in tissue loss. They are relatively common oral mucosa lesions that damage both the mucosa and the underneath connective tissue. Oral ulcers are frequently excruciatingly painful and are a common reason for a doctor's visit. Among the causes are infectious processes, neoplasms, gastrointestinal diseases, blood disorders, rheumatic diseases, immunological diseases, trauma lesions, and other variables. Due to the multiple variables that can cause them, a proper differential diagnosis is required. (Mortazavi H et.al, 2016)

1. Mouth Ulcer:

A mouth ulcer (also termed an oral ulcer or a mucosal ulcer) is an ulcer that occurs on the mucous membrane of the oral cavity. They are painful round or oval sores that form in the mouth, main Lyon the inside of the cheeks or lips.

Mouth ulcers, also known as aphthous ulcers, can be painful while eating, drinking or brushing teeth. Common causes of mouth ulcer include nutritional deficiency such as iron, vitamin especially Vitamin B12 and C, Poor hygiene of, infection stress, indigestion, mechanical injury, food allergies, hormonal imbalance, skin disease etc. A mouth ulcer is a break or breach in the mucous membrane, which is lines the inside of the mouth. It usually has yellow or white color and usually looks like a depression in mouth that is the mucous membrane. (Muñoz-Corcuera M et.al, 2009)

Fig No-1 Mouth Ulcer

2. Types of Mouth Ulcer:

On the basis of ulcer size and number,
Minor ulcers: These are around 2-8mm in diameter and they usually clear up in 10 days to 2 weeks.
Major ulcers: These are bigger and deeper, often with a raised or irregular border
Herpetiform ulcers: This type of ulcer is a cluster of dozens of smaller sores about the size of pin heads eder.
Ulcerative Conditions: Mouth ulcers are very common and are mainly due to trauma such as from ill- itting, Dentures, fractured teeth or fillings. (Wood NK et.al, 1997)

3. Factors responsible for the mouth ulcers:
Toothpastes and mouthwashes that contain sodium lauryl sulfate
Emotional stress/Psychic stress
Hormonal changes
Nutritional deficiencies
Mechanical trauma
Viral infections
Allergies and sensitivities
Genetics
Infectious agents (both bacterial and viral)
Medical condition

Gels:

Gels are typically semi-solid formulations having a liquid phase that has been thickened with other Components. Uses of topical gel preparations are for skin application or percutaneous penetration of medicament or local action to certain mucosal surfaces. The Commercially available gels containing synthetic and semisynthetic active agents which have several disadvantages like staining on the teeth, irritation, and burning sensation only because presence of high degree of alcohol content and some organic compounds. The present investigation deals with use of herbal powdered extract pomegranate peel, Tulsi leaves with lemon flavor in the treatment of mouth ulcer in pharmaceutical gel. (Greenberg MS et.al, 2008)

Fig No- 2 Gel

5. PLANT PROFILE

A. Punicagranatum

1.Origin:

Punicagranatum L. (pomegranate) is one of the oldest and known fruits native to Iran and surrounding areas and today widely cultivated in tropical and subtropical regions. There is a great interest worldwide in this fruit because of its potential health-promoting properties. (Dayakar MM et.al, 2012)

2. Biological Sources:

Dried Peels of Punicagrantum.
Part Used: peels
Synonym: Punica Nana L, Punica Florida Salisb.

3.Common Name

Sr. No	Language	Name
1)	Hindi	Anar
2)	English	Pomegranate
3)	Sanskrit	Dadimah
4)	Marathi	Dalimb

Table No-1 Common Name

4. Geographical sources:

The pomegranate is native to a region from modern-day Iran to northern India. Pomegranates have been cultivated throughout the Middle East, South Asia, and Mediterranean region for several millennia, and it is also cultivated in the Central Valley of California and in Arizona. (Neville BW et.al, 2002)

5. Taxonomical Classification:

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Rosidae
Order: Myrtales
Family: Punicaceae /Lythraceae
Genus: Punica
Species: Granatum

Fig No- 3 Punicagranatum tree

6. Uses:
Anti-inflammatory property
Analgesic Property.
Anticancer Property. Antioxidant Property.
Anti-microbial Property.
Anti-diabetic property.
Heart Disease.

B. Tulsi

1.Origin:
Tulsi is an aromatic shrub in the basil family Lamiaceae (tribe ocimeae) that is thought to have originated in north central India and now grows native throughout his thought world tropics Within Ayurveda, Tulsi is known as "The Incomparable One the easterm Medicine of Nature" and "The Queen of Herbs," and is revered as an "elixir of life" that is without equal for both its medicinal and spiritual properties... (Suomalainen A et.al, 2012)

2.Biological Sources:
Dried and fresh leaves of ocimum species like Sanctum L.
Dried Peels of Tulsi
Part Used: leaves
Synonym: Ocimum sanctum, Ocimum tomentosum

3.Common Name

Sr. No	Language	Name
1)	Hindi	Vrunda
2)	English	Holy Basin
3)	Sanskrit	Tulasi
4)	Marathi	Tulsi

Table No.2 Common Name

4. Geographical sources:

Tulsi grows in tropical and warm regions. Plant is originated in India and is distributed and cultivated In India plant is grown from Himalayas to Andaman and Nicobar Islands. It is widely grown in some areas of Asia and Africa; it grows naturally in moist soil. Size form and medicinal properties of the plant depend upon the type of the soil and variations in the rainfall. There are almost 150 species of Ocimum genus in the tropical regions of Asia throughout the country. It is cultivated up to 1800 m above the sea level 149. (Emopase FL et.al, 2004)

5.Taxonomical Classification:
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Laminas.

Family: Lamiaceae
Genus: Ocimum
Species: Ocimum sanctum

Fig No-4 Tulsi Tree

6.Uses:
Anti-inflammatory property
Anti-emetic Property.
Anti-cancer Property.
Anti-pyretic Property.
Anti-microbial Property.
Anti-fungal property
Mouth Infection.
Heart Disease.
Stress.
Headache.
Children's Ailments.
Digestion.
Reduce Cholesterol Level.
Reduce Blood Pressure.

C.Lemon

1.Origin:
It is native in north Indian but cultivated in Turkey, Mexico, United States, Argentina, Brazil, Italy, Spain and People Republic of China. The fruit of lemon can be used non-culinary and culinary purposes all over the world. Predominantly, lemon is used is juice from side to side the pulp and taste is as well used mostly in baking used cooking. (Roberts C et.al, 2005)

2.Biological Sources:
His obtained from the fresh ripe fruit of Citrus limon.
Synonym: lemon, leemu, nimbu
3.Common Name

Sr. No	Language	Name
1)	Hindi	Bara Nibu
2)	English	Citrus Lemon
3)	Sanskrit	Jamvira
4)	Marathi	Nimbu

Table No.3 Common Name

4. Geographical sources:
There are countless varieties of lemons grown throughout the world, with Argentina, Chuile, India, Mexico, and, of course, the U.S., being major growers of the commodity Lemon trees are evergreen. Flowering generally occurs during the spring. The

essential oil from lemon peel also has anti-microbial effects that can inhibit secondary infection in thrush. (Kolokotronis et.al, 2006)

5.Taxonomical Classification:
Kingdom: Plantae
Division: Magnoliophyta
Class: Dicotyledons
Order: Rosidae
Family: Rutaceae
Genus: Citrus
Species: Limetta

Fig No-5 lemon Tree

6. Uses:
Anti-oxidant
Anti-coagulant
Disinfectant
Preservative
Vasodilator
Laxative
Digestive
Scurvy
Anxiolytic effect
Skin care
Gout

7. Materials and Methods: -

1.Chemical: -
Carbopol 940, Propylene glycol, Methyl paraben, Propyl paraben, Triethanolamine.
1.Carbopol 940:
Chemical name: (C3H402)
Molecular weight: 72.02 g/mol
The Carbopol (Carbopol 940) is used as gelling agent in the present formulation study also ess some pharmaceutical activity.

Fig No -6 Carbopol 940

2.Propylene glycol:
Chemical name: $C3H8O2$
Molecular weight: 76.005 gm/mol
Propylene glycol is used as co-solvent

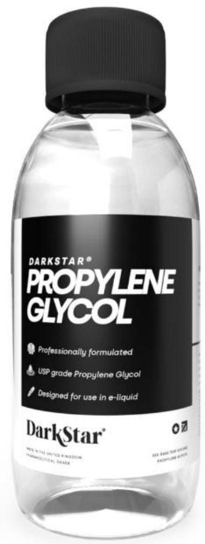

Fig no-7 Propylene Glycol

3. Methyl paraben:

Chemical name: methyl 4-hydroxybenzoate
Molecular weight: 152.15 gm/mol
Use: Antifungal Agent, Antimicrobial Agent, Stabilizer, Preservative

Fig No – 8 Methyl paraben

4. Triethanolamine:
Chemical name: C6H15NO3
Molecular weight: 149.188 g/mol
Use: Used for adjust pH of formulated aqueous gel.

Fig No-9 Triethanolamine

B. Glassware and Equipment's: Beaker, stand, thermometer, stirrer, weighing balance, digital PH meter, brook filled viscometer, Magnetic stirrer.

Fig No-10 Glassware

Methods:
1.Selection of plant: -
In the present study I have selected the plant of Punicagranatom, Tulsi Plant

2. Collection of plant material: -
The plant of Punicagranatum and Tulsi were collected from village of Aurangpur, Pune district, Maharashtra. The plant was Identified and Authenticated by CT Bora College of Arts, Commerce and Science College, shirur Dist-Pune.

3.Preparation of plant material: -
For the present study the fresh plant material was taken and it was wash and dried in shade. The leaves of tulsi were dried for 5 to 6 days for proper drying.

4. Preparation of powder: -
After drying it was pounded to coarse powder. Powdered drug was stored in air tight and light resistant container for the study.

5. Preparation of extract: -
Preparation of extract of powder 5gm in 50ml ethanol by using maceration method for 24 hours.

6. Phytochemical Screening:

Sr. No	Phytochemical test	Procedure	Observation	Punica granatom	Tulsi
1	Hager's Test	Filtrate + 1- or 2-ml reagent	Bright Yellow PPT	Present	Present
2	Mayers Test	Filtrate + 1- or 2-ml reagent	Creamson Colour ppt	Absent	Absent
3	Wagners Test	Filtrate + 1- or 2-ml reagent	Yellow Colour ppt	Present	Present
4	Dragendroffs Test	Filtrate + 1- or 2-ml reagent	Orange or Red Colour ppt	Present	Absent
5	Benedicts Test	0.5ml filtrate + reagent boil for 2 min	Pink colour solution	Absent	Absent
6	Fehlings Test	Sample + Fehlings A & B Heat	Red PPT	Present	Absent
7	Legals test	Sample dissolved in pyridine add sod. Nitropruside + 10% NaOH	Pink colour solution	Present	Absent
8	Ninhydrin test	Sample + reagent + Acetone	Purple colour	Absent	Absent
9	Foam test	Sample + water & shake	1cm Foam developed	Present	Present
10	Shinoda test	Sample + 5ml Alcohol + fragments of magnesium turning	Red colour	Present	Absent
11	Ferric chloride	Sample + few drops of 5% FeCl3	Dark green or Bluish black green	Present	Present
12	NH4OH test	0.4ml sample + 4ml 10% NaOH & shake	Emulsion Formation	Present	Present
13	Zinc Dust	Sample + Pinch of zinc dust Conc. HCL	Green or violet colour	Absent	Absent
14	Salkowski Test	Sample + Alcohol & conc. H2So4	Red colour	Present	Present

Table No.4 Phytochemical test

FORMULATION OF HERBAL MOUTH ULCER GEL

Ingredients	Quantity	Medicinal use
Punicagranatum Extract	2.5ml	Active ingredients
Tulsi Extract	1ml	Active ingredients
Methyl Paraben	0.01gm	Preservative
Carbopol 940	2.5gm	Gelling Agent
Triethanolamine	1-2 drop	PH & Buffer Adjusting agent
Lemon Oil	6-7drop	Fragrance
Propylene Glycol	2gm	Co-Solvent

Table No-5 Material use in Formulation Of Herbal gel

Procedure:

Carbopol 940dispersed in distilled water

↓

5ml water+ methyl paraben

↓

Heated on water bath

↓

After cooling propyl glycol

↓

Tulsi extract and punicagranatum extract was mix in above mix

↓

Volume make upto 20ml with distilled water

↓

Add lemon juice(flavour) into above mix

↓

Continuous stirring triethanolamine added drop-wise and adjust ph

Fig no-17 Formulated Herbal gel

Preparation of Herbal Mouth Ulcer Gel

Formula	F1	F2	F3	F4
Tulsi	3ml	1ml	1.5ml	2ml
Punicagranatum	2.5ml	2.8ml	2ml	2.5ml
Methyl Paraben	0.01gm	0.01gm	0.01gm	0.01gm
Carbopol 940	2.5gm	2gm	2gm	2.5gm
Triethanolamine	1-2drop	1-2drop	1-2drop	1-2drop
Lemon Oil	6-7drop	6-8drop	6-8drop	6-7drop
Propylene Glycol	2gm	1gm	1gm	2gm

Table No.6 Preparation of Herbal Mouth Ulcer Gel (4batches)

8. EVALUATION OF HERBAL GEL

Prepared Punicagranatum gel were evaluated for the following evaluation parameters Parameter:

1. **Physical Parameter**- Appearance and colour were examined by Visual Inspection.
2. **Microscopic Analysis** -Microscopic study by optic microscope with magnification of 10 and 40 for uniformity, gel texture & bubbles.
3. **Clarity of gel-** The clarity of all the gel batches was determine by visual inspection.

4. Spreadability:

Spreadability was determined by the apparatus which consists of a wooden block, which was provided by a pulley at one end. By this method spreadability was measured on the basis on slip and drag characteristics of gels. An excess of gel (about 2gm) under study was placed on this ground side. The gel was then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A one kg weighted was placed on the top of the two slides for 5 min.

to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped off from the edges. With the help of string attached to the hook and the time (in sec.) required by the top slide to cover a distance be noted. A shorter interval indicates better Spreadability**.** (Wald A et.al, 1995)

Formula:
Spread ability was calculated using the following formula

SML/T

Where,
S- Spreadability,
M-Weight in the pan (tied to upper slide),
L-Length moved by the slide
T-Time (in sec)

Fig. No. 19 Spreadability

5.Homogeneity:
Gel formulations were tested for homogeneity by visual inspection after the gels have been set in to the container. They were tested for their presence and appearance of any aggregates Homogeneity of gel formulation was reported (Woo SB et.al, 1997)

6. Gel Strength:
Gel strength was determined by the time in seconds required by the weight to penetrate in the gel. A Sample amount of 5 gm of each of the optimize batches was taken and 3.5 gm weight was placed on the surface of gel. The time in seconds required by the weight to penetrate 0.5 cm in the gel. (Mueller NH et.al, 2008)

7. PH Determination:
The pH of developed gel formulations was determined using digital pH meter. 1gm of gel was dissolved in 100 ml distilled water and kept aside for 2 hours. The measurement of pH of each formulation was done in triplicate and average values are calculated**.** (Palencia LA et.al, 2003)

8. Stability study:
Stability studies were done with open and close container. Here, by subjecting the product to room temperature for 1 month.

9. Viscosity:
Viscosity was determined by using Brookfield viscometer spindal no.1 (5-62, modelL.VDV-E) at 33degree celcius with a spindal speed of the viscometer rotated at 6rpm. (Lee SI et.al, 2008)

10.Anti-microbial Activity:
vitro anti-bacterial study of formulated paste was performed by dise diffusion method by using against a pathogenme bacterial strain S aureus, S aureus was initially cultured cells were tend to multiple in the agar plates. Initially plates were streaked with inoculum; bores with rotated never into the medium e agar plate formulated paste sand an equal distribution of itocantk borer. The surface of bore Then the formulated paste and marketed formulations were places present around the Bultured plates. The plates were wrapped with paraffin, labelled, and incubated at 37°C for the 24 hour. Each plate was examined after incubation for 24 hrs. The diameter of Inhibition (ZOI) measured in millimeters (mm) with a ruler. (Romier B et.al, 2008)

Fig. No.22: Anti-Microbial Activity

9. RESULT AND DISCUSSION

The results of evaluation parameter in vitro study shows in tablet below

1.Organoleptic Evaluation:

Colour	
Odour	Characteristics
Homogenecity	good

Table No. 7: Organoleptic Evaluation results

From the above mention results in table, it is clearly shows that prepared gel formulation good appearance. The gel formulation have good homogenecity.

2 Stability Study:

Open Container	Closed
Not stable	stable

Table No. 8: Stability Study results

One month stability study was done with open and close container and it's showed that open container containing gel was not stable and close container gel was stable. Formulated gel containing open container when pose to ambient room temperature then syneresis was observed it means the contraction of gel by separating d of liquid. Syneresis, it means the form of instability in aqueous gels. (Quachrif A et.al, 2012)

3. Spreadability:

Sr.no	Type of Evalution	Results
1	Spredability	4+0.1

Table No -9 spreadability Result

4.PH

Sr.no	Type Of Evalution	Results
1	Ph	5.96

Table no-10 Ph Result

5. Gel strength:

Sr.no	Type of evalution	Results
1	Gel Strength	38+0.7

Table No. 11: Gel strength Result

6.Viscosity:

Sr.no	Type of evalution	Results
1	Viscosity	1000

Table No. 12: viscosity Result

From the above table it is clearly show that the pH of formulated gel was found in suitable range. The spreadability show that with increasing viscosity of formulation spreadability decreases and vice-Versa. Gel strength of gel was found in suitable range. (Chavan M et.al, 2012)

7.Anti-Microbial activity:

The gel formulation shows anti-bacterial and anti-microbial activity against Saureus. S. aureus is the main micro-organism to treat mouth ulcer and formulation it can also use to treat mouth ulcer treatment. (Rogers RS et.al, 1997)

10.Conclusion:

From the mentioned I results, it was concluded that the prepared gel Formulation are in good appearance with suitable PH range. Formulated gels have good homogeneity, proper gel strength and Spreadability. The gel is neither too thick or too thin. The all formulated gels are found to be stable in close container as compare to open container. The, formulation showed the antibacterial activities against S.aureus and E-coli. Tulsi extract shows anti-microbial activity S.aureus.

Therefore, the study concluded that the natural remedies are more acceptable & they are safer with minimum side effects than synthetic preparations.

Thus, the data presented in this study, it was concluded that the formulated gel of extract of pomegranate peel powder and tulsi leaves powder with lemon flavor possesses a significant therapeutically efficacious & have suitable vehicle for drug delivery.

Thus, the formulated gel is suitable for treatment of mouth ulcer.

Result:

Sr. No	Phytochemical test	Procedure	Observation	Punica granatom	Tulsi
1	Hager's Test	Filtrate + 1- or 2-ml reagent	Bright Yellow PPT	Present	Present
2	Mayers Test	Filtrate + 1- or 2-ml reagent	Creamson Colour ppt	Absent	Absent
3	Wagners Test	Filtrate + 1- or 2-ml reagent	Yellow Colour ppt	Present	Present
4	Dragendroffs Test	Filtrate + 1- or 2-ml reagent	Orange or Red Colour ppt	Present	Absent
5	Benedicts Test	0.5ml filtrate + reagent boil for 2 min	Pink colour solution	Absent	Absent
6	Fehlings Test	Sample + Fehlings A & B Heat	Red PPT	Present	Absent
7	Legals test	Sample dissolved in pyridine add sod. Nitropruside + 10% NaOH	Pink colour solution	Present	Absent
8	Ninhydrin test	Sample + reagent + Acetone	Purple colour	Absent	Absent
9	Foam test	Sample + water & shake	1cm Foam developed	Present	Present

10	Shinoda test	Sample + 5ml Alcohol + fragments of magnesium turning	Red colour	Present	Absent
11	Ferric chloride	Sample + few drops of 5% FeCl3	Dark green or Bluish black green	Present	Present
12	NH4OH test	0.4ml sample + 4ml 10% NaOH & shake	Emulsion Formation	Present	Present
13	Zinc Dust	Sample + Pinch of zinc dust Conc. HCL	Green or violet colour	Absent	Absent
14	Salkowski Test	Sample + Alcohol & conc. H2So4	Red colour	Present	Present

Fig. No.1. Mayers Test

Fig. No.2. Ferric Chloride Test

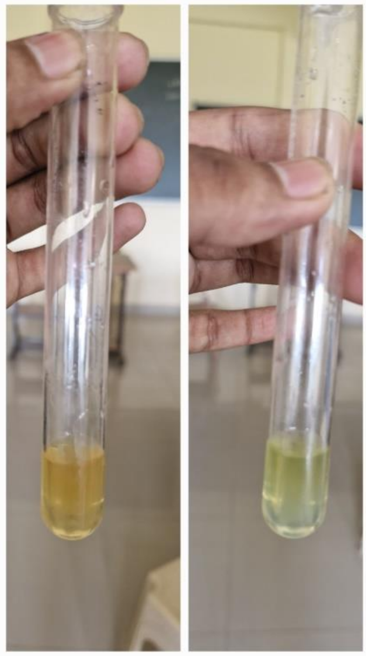

Fig No.3. Wagnar Test

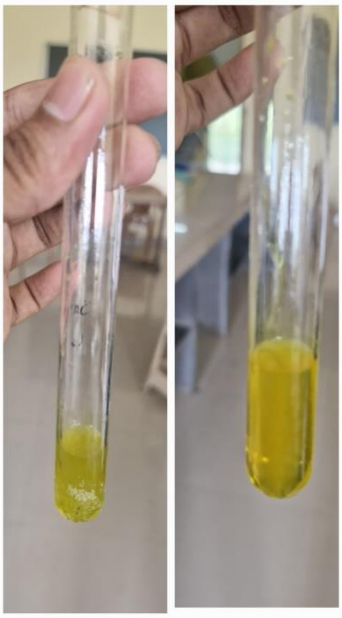

Fig. No.4. Hagers Test

Fig. No.5. Draondroff Test

Fig. No.6. Shinoda test

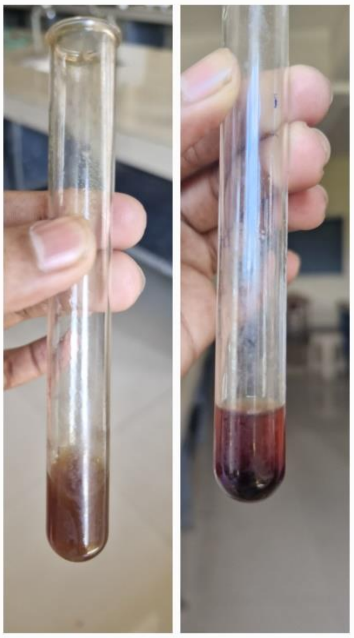

Fig. No.7. Salkowoski Test

Fig. No.8. Benidic Test

Fig. No.9. Saponin Test

Fig. No.10. Zinc Test

Fig. No.11. Magnesium turning Test

Fig. No.12. NH4OH Test

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