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LANTANA CAMARA: A HERBAL EXTRACT ORAL SUSPENSION FORMULATION AND EVALUATION FOR ITS ANTI-TUSSIVE ACTIVITY

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ABSTRACT
In the present investigation, two types of orally administrable dosage forms of leaves and flowers of *lantana camara* extracts were developed. Two formulations from liquid class were designed and formulated. By considering difficulty of solubility of herbal drugs in a vehicle, in one of the liquid class, decoction form of drugs in specific vehicle was used. This form of drugs hereafter considered as Liquid Oral Dosage Form. To prepare a liquid dosage in suspension form was also designed using acacia and tragacanth as suspending agents into four formulations. Formulated dosage forms are then subjected to evaluation parameters. The liquid oral form was evaluated for parameters like $p^{H,}$ specific gravity, density and stability studies. While the suspension form was evaluated for the above parameters along with rate of sedimentation and viscosity. Out of four formulations LS2 formulation was found to shows the best results, which is better than LS1, LS3 and LS4 form of suspension.

KEYWORDS: Lantana Camara, Liquid Oral Dosage form, Herbal Formulations, Evaluation.

INTRODUCTION TO HERBAL DRUGS
Herbs are nature's gift to mankind and an herbal renaissance is blooming a cross the world. Medicinal herbs contain substances known to modern and ancient civilizations for their healing properties. They have been important to mankind, both socially and economically, for thousands of years.[1]

Most of the modern medicines have originated from plant metabolites. Herbal medicines have become more popular in recent years because it is believed that these do not show many side effects, adverse or toxic effects compared to synthetic medicines. Biological scientists have played equally significant role in originating meaningful screening and testing models and in the overall evaluation of new agents.[2]

Liquid Solution
Liquid preparations for **oral** use are usually solutions, emulsions or suspensions containing one or more active substances in a suitable vehicle.[3]

Suspension
A suspension is a heterogeneous mixture containing solid particles that are sufficiently large for sedimentation.[4]

A suspension is often chosen as pharmaceutical dosage form for drugs insoluble in water and aqueous fluids at the dosage required for administration and when attempts to solubilize the drug would compromise stability and safety. The large surface areas of the dispersed drug particles often facilitate absorption. Unlike drug particles contained in tablets or capsules, the dissolution of drug particles in suspension and subsequent absorption commence upon dilution in gastrointestinal fluids. Finely divided particles dissolve faster and have higher relative solubility than do similar macro particles.[5]

AIM OF THE STUDY
The aim of this work is to formulate and evaluate the herbal extraction of Lantana camara as a liquid oral suspension. Liquid oral is prepared using decoction method and suspension by using acacia and tragacanth as suspending agents.

OBJECTIVES
- Collection of aerial parts (leaves and flowers) of Lantana camara
- To prepare the decoction of leaves and flowers of Lantana camara.
- Selection of the excipients for suspension form (acacia and tragacanth)
- Preparation of liquid oral suspension of Lantana camara
- Evaluation tests like pH, specific gravity, density, viscosity, rate of sedimentation, and stability studies for liquid form of herbal extract.

Plan of Work

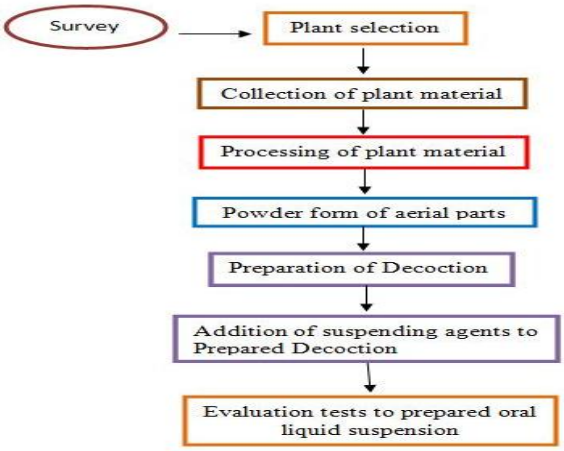

Figure. 1: Flow chart of plan of work.

Plant Profile: Lantana Camera

Lantana camara, also known as big-sage (Malaysia), wild-sage, red-sage, white-sage (Caribbean) and tickberry (South Africa),[6] is a species of flowering plant within the verbena family,Verbenaceae, that is native to the American tropics.[4,7] *Lantana camara*, often planted to embellish gardens, has spread from its native Central and South America to around 50 different countries.[8]

Figure. 2: Lantana camera.

Taxonomical Description

Kingdom: Plantae
Order: Lamiales
Family: Verbenacea
Genus: Lantana
Species: Camara

Figure-3 Taxonomical Description.

General Description: *Lantana camara* is a small perennial shrub which can grow to around 2 m tall and form dense thickets in a variety of environments.[9] *Lantana camara* has small tubular shaped flowers which each have four petals and are arranged in clusters in terminal areas stems. Flowers come in many different colours including red, yellow, white, pink and orange which differ depending on location in inflorescences, age, and maturity.[10] After pollination occurs the colour of the flowers change (typically from yellow to orangish, pinkish, or reddish), this is believed to be a signal to pollinators that the pre-change colour contains a reward as well as being sexually viable, thus increasing pollination efficiency.[11] The leaves are broadly ovate, opposite, and simple and have a strong odour when crushed.[12] The fruit of *L. camara* is a berry-like drupe which turns from green to dark purple when mature. Both vegetative (asexual) and seed reproduction occur. Up to 12,000 fruits can be produced by each plant.[13]

Figure-4 lantana camara.

Distribution: The native range of *L. camara* is Central and South America, however it has become naturalized in around 60 tropical and sub-tropical countries worldwide.[14,15] It is found frequently in East and South Africa where it occurs at altitudes below 2000 m and often invades previously disturbed areas such as logged forests and areas cleared for agriculture.[16]

Habitat: Lantana camara is found in a variety of environments, including: Agricultural areas, Forest margins and gaps, Riparian zones, Grasslands, Secondary forest, and Beach fronts. Lantana camara is rarely found in natural or semi-natural areas of forest as it is unable to compete with taller trees due to its lack of tolerance for shade,[4] and instead grows at the forest edge. Lantana camara can survive in a wide range of climatic conditions, including drought, different soil types, heat, humidity and salt. It is also relatively fire tolerant and can quickly establish itself in recently burnt areas of forest.[16,17]

Pharmacological and biological activity

The *Lantana camara* plant has been used to treat a wide variety of disorders. It was found to use in folk remedies for cancers and tumours. In Central and South America, the leaves were made into a poultice to treat sores, chicken pox and measles. In Asian countries, leaves were used to treat cuts, rheumatism, ulcers and as a vermifuge. Decoctions were applied externally for leprosy and scabies. *L.camara* also used to treat cold, rheumatisms, asthma and high blood pressure with preparations from the plant. A tea prepared from the *Lantana camara* leaves and flowers was taken against fever, influenza and stomach-ache. In Ghana, infusion of the whole plant was

used for bronchitis and the powdered root in milk was given to children for stomach-ache.

Other than that, *Lantana camara* is having Anthelmintic activity, Wound healing activity, Larvicidal activity and Anti-Tussive activity.

In this project my work done majorly explains about Anti-Tussive activity of *Lantana camara* leaves and flowers extraction. Medicinal plants are potential source of substances with high- Anti-Tussive efficiency with minimal unwanted effects.[1]

Coughing may be initiated either voluntarily or reflexively. Hydration of respiratory tract by steam inhalation, demulcents are effective in reducing symptoms in the majority of cases but, for uncontrolled cough, opioidergic central cough suppressants are used. However, their greatest disadvantage is a high rate of unwanted effects, like depression of the respiratory centre, decreased secretion in the bronchioles, and inhibition of ciliary activity.[18]

Excipient Profile: Tragacanth

Gum tragacanth is a viscous, odorless, tasteless, water-soluble mixture of polysaccharides obtained from sap which is drained from the root of the plant and dried. The gum seeps from the plant in twisted ribbons or flakes which can be powdered. It absorbs water to become a gel, which can be stirred into a paste. The gum is used in vegetable-tanned leatherworking as an edge slicking and burnishing compound, and is occasionally used as a stiffener in textiles. The alkaloid it contains[19] has been used historically as a herbal remedy for such conditions as cough and diarrhea. As a mucilage or paste, it has been used as a topical treatment for burns.[20]

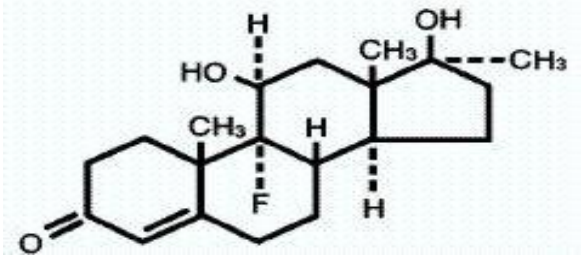

Figure. 5: Chemical Structure of Tragacanth.

Figure. 6: Tragacanth.

Acacia: Acacia is the dried gummy exudation from Acacia senegal and other species of Acacia (family Leguminosae), prepared as a mucilage and syrup. Acacia, also known as gum Arabic, is used in the pharmaceutical industry as an emulsifier, stabilizing agent, suspending agent, binder, and viscosity-increasing agent.[21]

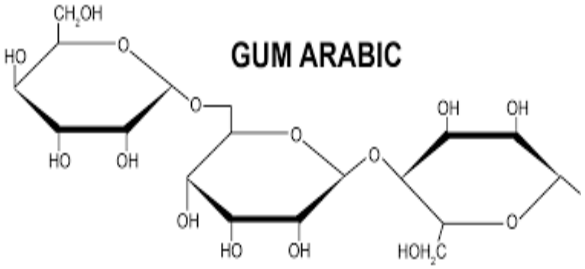

Figure-7 Chemical Structure of Acacia.

Figure-8 Acacia.

MATERIALS AND METHODS

Materials Used

Table. 1 List of materials used and their source.

S. No	Ingredients	Manufacturer
1.	Lantana camara	Local market
2.	Acacia	Sd fine-chem Ltd.(**SDFCL**)
3.	Propylparaben	Qualikems fine chem Pvt Ltd.
4.	Glycerol	Sd fine-chem Ltd.(**SDFCL**)
5.	Sucrose	Sd fine-chem Ltd .(**SDFCL**)
6.	Sorbitol	Sd fine-chem Ltd.(**SDFCL**)
7.	Methylparaben	Qualikems fine chem Pvt Ltd.

Instruments (Or) Equipments Used

Table. 2 List of equipment's used and their source.

S. NO	EQUIPMEMTS	MANUFACTURER
1.	pH meter	Digisun ElectronicsModel no:707
2.	Ostwald viscometer	Borosil
3	Pycnometer	Borosil
4	Measuring cylinder	Borosil

METHODOLOGY

Collection

Lantana camara leaves and flowers were collected from local market of Nalgonda, Nalgonda dist., Telangana, India. All plant materials were collected from the months of December to January 2016-17.

Extraction

Extraction, as the term is used pharmaceutically, involves the separation of medicinally active portions of plant or animal tissues from the inactive or inert components by using selective solvents in standard extraction procedures. The products so obtained from plants are relatively impure liquids, semisolids or powders intended only for oral or external use. These include classes of preparations known as decoctions, infusions, fluidextracts, tinctures, pilular (semisolid) extracts and powdered extracts. Such preparations popularly have been called galenicals.

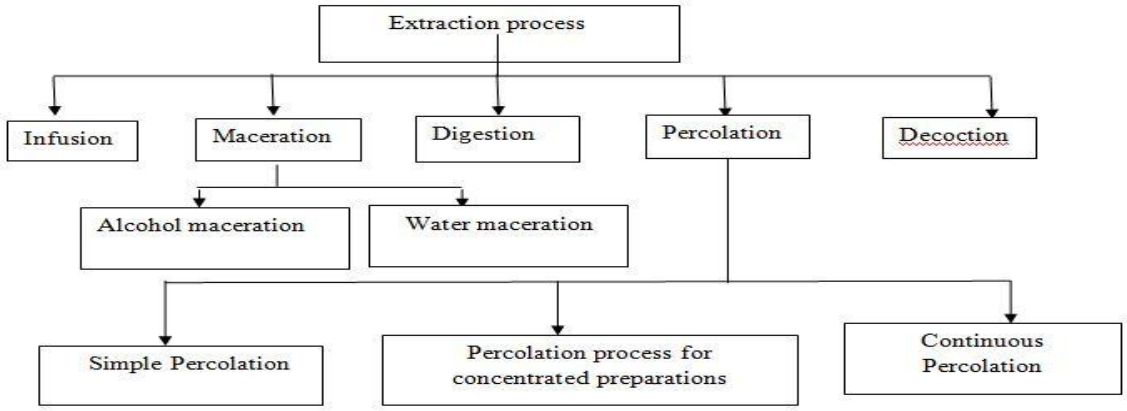

Figure. 9: Flow chart of different extraction process.

Formulation for Different Suspension of Extract

S. No	Ingredients	Formulations			
		LS1	LS2	LS3	LS4
1	Extract	50 gm	**50gm**	50 gm	50 gm
2	Sorbitol Solution {0.5 %}	5 ml	**5 ml**	5 ml	5 ml
3	Glycerine	25 ml	**25 ml**	25ml	25ml
4	Aqueous Tragacanth Solution (1.25 %)	5 ml	**10 ml**	-	-
5	Aqueous Acacia Solution (1.25 %)	-	**-**	5ml	10ml
6	Methyl Paraben	0.9 gm	**0.9 gm**	0.9 gm	0.9 gm
7	Propyl Paraben	0.3 gm	**0.3 gm**	0.3 gm	0.3 gm
8.	Purified water	Upto100ml	**Upto100ml**	Upto100ml	Upto100ml

Preparation of *lantana camara* oral suspension as liquid dosage form

This preparation is majorly includes two steps

A} preparation of liquid oral

B} preparation of herbal suspension dosage form

A} Preparation of Liquid Oral

To prepare Liquid Oral form of flowers and leaves of *L.camara* following steps were carried out

a) Method of Preparation of Decoction- 500 g each of powder of leaves and flowers of *L.camara* was taken. Powder was mixed with 4000ml (4 litres) of water. The powdered material was boiled until total volume become one fourth of previous. After boiling liquid was cooled and filtered. Filtrate was taken to prepare final Liquid Oral form.

b) Method of Preparation of Simple Syrup

850 g. of sucrose was dissolved in sufficient water to get 1000 ml of concentrated simple syrup. Then the solution was filtered. This simple syrup was used as vehicle.

c) Method of preparation of final Liquid Oral form

To prepare final Liquid Oral of *L.camara* One part of

decoction was mixed with five parts of Simple Syrup (1: 5). Solubility was checked by observing the clarity of solution visually. The final Liquid Oral form of *L.camara* was then subjected to evaluation of different parameters as per official standards.

B} Preparation of Herbal Suspension dosage form
The fine extract particles were properly mixed by triturating. 5 ml of sorbitol solution was mixed with 25 ml of glycerin. The powdered form of drugs was wetted thoroughly with Sorbitol and Glycerin solution to reduce liquid–air interfacial tension.

The suspending agents like tragacanth and acacia in the aqueous medium containing selected preservatives were then added in to the wetted mass slowly, with continuous triturating. Four possible formulations of Suspension viz. LS1, LS2, LS3 and LS4 were prepared by using 5ml, 10ml of 1.25% aqueous tragacanth and acacia solution respectively. Finally, suspension brought up to the final volume with purified water by continuous trituration so as to get uniform product. All four formulations of suspension were then subjected to evaluation of production quality as per official standards.

Evaluation of Lantana Camara Extract Suspensions
a. Evaluation of Liquid Oral the different parameters of decoction and final Liquid Oral were assessed such as pH, specific gravity and density, stability study of final Liquid Oral was carried out at different temperature and at relative humidity.
b. Evaluation of Suspension The four forms of Suspension (S1, S2, S3 and S4) were evaluated for rate of sedimentation, pH, specific gravity and density, viscosity, stability study of the final suspension was carried out.

pH: pH (potential of hydrogen) is a numeric scale used to specify the acidity or basicity of an aqueous solution. A pH Meter is a scientific instrument that measures the ion activity in water-based solutions, indicating its acidity or alkalinity expressed as pH.

Viscocity: The internal property of a fluid for its resistance to flow is known as viscosity.

Specific Gravity: Relative density, or specific gravity, is the ratio of the density (mass of a unit volume) of a substance to the density of a given reference material. Specific gravity usually means relative density with respect to water.

Sedimentation: Sedimentation means settling of particle (or) floccules occur under gravitational force in liquid dosage form. Velocity of sedimentation expressed by Stoke's equation.

$$vsed=d2(\rho s-\rho o)g/18\,\eta o$$

Where, d = Diameterof particle
r = radius of particle
vsed= sedimentation velocity in cm / sec
ρs= density of disperse phase
ρo= density of disperse media
g = acceleration due to gravity
ηo = viscosity of disperse medium in poise

Sedimentation Parameters Sedimentation volume (F) or height (H) for flocculated suspensions
Definition: Sedimentation volume is a ratio of the ultimate volume of sediment (Vu) to the original volume of sediment (VO) before settling.
F = V u / VO

Where, Vu = final or ultimate volume of sediment
VO = original volume of suspension before settling
F has values ranging from less than one to greater than one.

When F < 1 then Vu< Vo, When F =1 then Vu = Vo The system is in flocculated equilibrium and show no clear supernatant on standing.

When F > 1 then Vu > Vo Sediment volume is greater than the original volume due to the network of floccs formed in the suspension and so loose and fluffy sediment.

The sedimentation volume gives only a qualitative account of flocculation.

Figure. 10 Rate of Sedimentation.

Degree of flocculation (β) It is the ratio of the sedimentation volume of the flocculated suspension, F, to the sedimentation volume of the deflocculated suspension.

ß = F / F ∞
ß = (Vu/Vo) flocculated / (Vu/Vo) deflocculated
The minimum value of ß is 1, when flocculated suspension sedimentation volume is equal to the sedimentation volume of deflocculated suspension.

Stability Studies
The purpose of stability testing is to provide the evidence for the quality of drug substance or drug product, and how it varies with time under the influence of environmental conditions (heat, humidity, light, air etc.).

RESULTS

Table. 4: ICH guidelines for stability study.

Study	Storage conditions	Time period
Accelerated	40º C±2º C / 75%±5% RH	3months
Intermediate	30º C±2º C / 65%±5% RH	6months
Long term	25º C±2º C / 60%±5% RH	12months

Table. 5: Quantitative Evaluation of Liquid Oral Form of Herbal extract.

S. No	Parameters	Observed Values
1.	pH of Decoction	5.90
2.	Specific Gravity of Decoction	1.027g/ml
3.	Density of Decoction	1.25 g/cm3
4.	pH of Final Liquid Oral	6.0
5.	Specific Gravity of Liquid Oral	1.174g/ml
6.	Density of Liquid Oral	1.28 g/cm3

Table. 6 Quantitative Evaluation of Suspension Form Herbal extract.

S. No	Parameters	Observed Values			
		LS1	LS2	LS3	LS4
1	pH of Suspension	4.3	5.5	4.0	4.5
2	Specific gravity (g/ml)	1.1068	1.1071	1.1067	1.1065
3	Density (g/cm3)	1.0248	1.0247	1.0123	1.0221
4	Viscosity (cp)	0.0051	0.0095	0.0049	0.0050

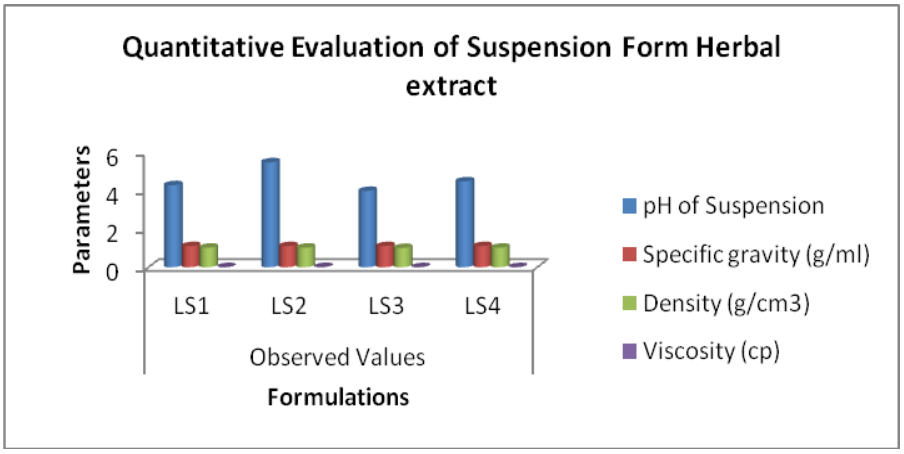

Figure. 11: Quantitative Evaluation of Suspension Form Herbal extract.

Table. 7: Rate of Sedimentation values of tragacanth.

S. No	Time (min)	Total volume v0	LS1		LS2	
			Ultimate volume vu	Vu/vo =f	Ultimate volume vu	Vu/vo =f
1.	0	100 ml	100 ml	1	100ml	1
2.	5	100 ml	70 ml	0.7	80 ml	0.8
3.	10	100 ml	50 ml	0.5	65 ml	0.65
4.	15	100 ml	40 ml	0.4	25 ml	0.25
5.	30	100 ml	30 ml	0.3	20 ml	0.20
6.	45	100 ml	27 ml	0.27	23 ml	0.23
7.	60	100 ml	25 ml	0.25	21 ml	0.21

Table. 8: Rate of Sedimentation values of Acacia.

S.no	Time (min)	Total volume v0	LS3		LS4	
			Ultimate volume vu	Vu/vo =f	Ultimate volume vu	Vu/vo =f
1.	0	100 ml	100 ml	1	100ml	1
2.	5	100 ml	92 ml	0.92	93ml	0.93
3.	10	100 ml	80ml	0.80	85ml	0.85
4.	15	100 ml	78ml	0.78	80ml	0.80
5.	30	100 ml	65ml	0.65	68ml	0.68
6.	45	100 ml	45ml	0.45	55ml	0.55
7.	60	100 ml	31ml	0.31	39ml	0.39

Table. 9: Rate of Sedimentation values for all the four formulations.

S. No	Time (min)	Total volume v0	LS1 Vu/vo =f	LS2 Vu/vo =f	LS3 Vu/vo =f	LS4 Vu/vo =f
1.	0	100 ml	1	1	1	1
2.	5	100 ml	0.7	0.8	0.92	0.93
3.	10	100 ml	0.5	0.65	0.80	0.85
4.	15	100 ml	0.4	0.25	0.78	0.80
5.	30	100 ml	0.3	0.20	0.65	0.68
6.	45	100 ml	0.27	0.23	0.45	0.55
7.	60	100 ml	0.25	0.21	0.31	0.39

Table. 9: Results of Stability Test of Suspensions.

S. No.	Sample No.	Time Duration (hr)	Temperature (°C)	Turbidity/Homogeneity	Color/Odor
1.	A1	24	4°C	X	No Change
2.	B1	24	RT	X	No Change
3.	C1	24	47°C	X	No Change
4.	D1	24	60°C	X	No Change
5.	A2	48	4°C	X	No Change
6.	B2	48	RT	X	No Change
7.	C2	48	47°C	X	No Change
8.	D2	48	60°C	X	No Change
9.	A3	72	4°C	X	No Change
10.	B3	72	RT	X	No Change
11.	C3	72	47°C	X	No Change
12.	D3	72	60°C	X	No Change

DISCUSSION

The primary objective of this work was to formulation and evaluation of oral herbal liquid dosage form i.e., liquid oral and suspension of *Lantana camara* extract. The development of such formulations will mark an important advancement in the area of phytopharmaceuticals. The present investigation examines formulation design & evaluation of liquid oral herbal dosage form. The liquid oral herbal dosage forms like Liquid Oral & Suspension prepared showed good elegance. The Liquid Oral was evaluated for parameters like measurement of pH, specific gravity, density & stability. While the suspension form was evaluated for the above parameters along with rate of sedimentation, viscosity.

The herbal Form of LS2 formulation shows the better results compare to other 3 formulations. PH of LS2 is 5.5 and specific gravity 1.1071 g/ml, density 1.0247g/cm3, viscosity 0.0095cp. Four possible forms of suspension were evaluated for sedimentation ratio. LS2 form of suspension shows sedimentation ratio 0.21 after 60 min. which is better than LS1, LS3 and LS4 form of suspension. All forms of suspension although shows easily dispersible pattern.

The developed suspension was evaluated for stability studies for 24, 48 and 72 hours with varying temperature of 4°C, Room temperature and 47°C, 60°C. There was no change observed in either colour or odor of the formulated suspension. It did not produce turbidity at lower temperature of 4°C. It was clear homogenous liquid without turbidity at higher storage temperature of 60°C too. Thus it can be concluded that the herbal syrup was the suitable form which was developed.

CONCLUSION

Oral herbal dosage forms of *lantana camara* leaves and flowers, into Liquid Oral Suspension showed good elegance & palatability. Liquid dosage forms like Liquid

Oral Suspension having good stability on storage. Thus it can be concluded that these combined oral herbal dosage forms could be suitable dosage form for *lantana camara*. By considering difficulty of solubility of herbal drugs in a vehicle, in one of the liquid class, decoction form of drugs in specific vehicle was used. This form of drugs hereafter considered as Liquid Oral Dosage Form. To prepare a liquid dosage in suspension form was also designed using acacia and tragacanth as suspending agents into four formulations. Formulated dosage forms are then subjected to different evaluation parameters.

Among all the formulations LS2 were considered best as it has appropriate concentration of aqueous tragacanth solution 100ml and having the pH (5.5), Density (1.0247g/cm^3), specific gravity (0.1071g/ml) viscosity (0.0095cps)and sedimentation ratio of suspension shows 0.21 after 60 min. The results of stability study of suspension of drugs indicate the homogeneity of syrup without turbidity at storage temperature and fulfilling all the parameters satisfactorily. The herbal product is in high demand because of the least possibilities of side effect. The present studies help to develop an herbal cough syrup, which is effective and safe.
Thus it can be concluded that these oral herbal dosage forms could be suitable dosage form for *Lantana camara* extract for commercial purpose.

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