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Research Article

# FORMULATION DEVELOPMENT AND EVALUATION OF HERBAL JELLY

**Thombre Nilima*, Ahire Priyanka.S, Kshirsagar Sanjay, Attarde Daksha**

Department of Pharmaceutics, MET's Institute of Pharmacy, Adgaon, Nashik, 422003. Savitribai Phule Pune University, Pune (Maharashtra), India.

*For Correspondence:
Department of Pharmaceutics, MET's Institute of Pharmacy, Adgaon, Nashik, 422003. Savitribai Phule Pune University, Pune (Maharashtra), India.

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**ABSTRACT**

Natural products are diverse sources of important chemical constituents. In the present study, the Justicia adhatoda plant was selected from the family Acanthaceae. Having bronchodilation, expectorant and antimicrobial activity. The optimized batch was evaluated by in vitro method of % extract release shown in results. The formulation was prepared by the heating and Congealing Technique using 32 full factorial designs were applied for the optimization of the process parameters including Concentration of amount of gelatin and propylene glycol were selected as independent variables. The dependent variables viscosity and % drug release as responses. Each factor considered at -1, 0, +1 level. Mathematical equations and response such as surface plots were used to relate was taken dependent variables with independent variables. The optimization model predicted a yield of viscosity 3808cp and percentage drug release (1 hour) at 94.16%.

**KEY WORDS**: Justicia adhatoda, bronchodilator, physicochemical method, factorial designs, optimization.

## INTRODUCTION

### *JUSTICIA ADHATODA (Malabar nut tree)*

*Justicia adhatoda* (AV) is known as *Malabar nut tree* belonging to family (Acantaceae). Plant Leaves, roots and young plants of AV contain the quinazoline alkaloids like (vasicine, 7-hydroxyvasicine, vasicinolone, 3deoxyvasicine, vasicolinone, triterpenes, anisotine) betaine, steroids carbohydrate and alkanes. In the flowers contain triterpenes (a-amirine), and flavonoids (Apigenin, astragalin, kaempferol, quercetin, vitexin) have been found *Justicia adhatoda* , is Malabar nut tree is part of the family Acanthaceae. (1)

**Fig 1. JUSTICIA ADHATODA (1)**

Plant is small evergreen, sub-herbaceous plant bush distributed throughout India, especially in the lower Himalayas (up to 1300 meters above sea level) it is cultivated in India, Sri Lanka, Burma and Malaysia. In Ayurveda, Indian medicine it is commonly known as vasica is plant in indigenous system of medicine. Plant grows to about a height of 1.5-2.0m with leaves about 1015cm long & 5.0cm wide & white or purple flowers & 4-seeded fruits. The leaves are of dark green colors above & pale yellow below. Flowers are typical, white arranged in pedunculated spike. Adhatoda leaves is used as extensively in the Ayurvedic Medicine for over 2000 years in respiratory disorders. Medicinal plants have play a key role in the world health care systems. Roots, leaves & flowers are the active principles of the plant possess a number of pharmacological properties & they are used in cough, chronic bronchitis, rheumatism, asthma & bronchial asthma. Plant leaves and roots it contain several alkaloids (mainly contain quinazoline alkaloid, vasicine and vasicinone, vasicinolone and vasicol), Bronchodilator effect of the bronchii. The activity on bronchii is sedative, expectorant, antispasmodic, anthelmintic, bronchial antiseptic and bronchodilator. Leaf extract formulation used in the treatment of bronchitis and asthma for many centuries in various country. It relieves respiratory cough and breathlessness. Individual plant extract was qualitative phytochemical screening for the presence of some chemical constituents. (1). Justicia adhatoda is important for the Ayurvedic medicinal plant herb. The whole parts of plant from root to leaves are using to treat many disorders. Leaves is great importance in treatment of respiratory disorder. The plant is more effective in treatment of asthma, bronchitis, tuberculosis and other disorders. Justicia adhatoda is plant are used as medicine in Ayurveda, Siddha, Homeopathy, Unani and other ancient system of the medicine. This product are approved by many doctors world. Plant is more used to treting expectorant, antiseptic, anthelmintic, antispasmodic, and mainly as respiratory bronchi.

Justicia adhatoda is a most prominent medicinal plant herb. They are plant leaves, flower, and root, fully plant is used in many drug formulations. Justicia adhatoda plant is a high, dense, with large, much-branched, evergreen shrub, lance-shaped leaves. AV plant flowers in dense, short points; stem of the tips shorter than leaves. Plant leaf structures called husks, present on the poits; these are pointedly veined. (2)

**Medicinal uses**

The drug Vasaka plant comprises to the fresh or dryer leaves of the plant. Pant leaves include an alkaloid is due to vasicine, and essential oil. The head use of Vasaka is expectorant, those given in the form of juice, syrup or essence. It mollifies the dense sputum and facilitates it is coming out and fast relaxation in bronchitis. The expectorant activity is the incentive of bronchial glands.

**Chemical composition**

The plant leaves of Justicia adhatoda contain the phyto-chemicals contain such as tannins, alkaloids, flavonoids, saponins, and phenolics. Leaves include vasicine, is a quinazoline alkaloid and essential oil. It further need other chemicals such as Luteolin, Adhatodic acid, Tritriacontane, B- Sitosterol, Kaempferol, 3- Sophoroside, q- Hydroxyvasicinine, Vit –C, vasicol. Vasicinol, Vaicinolone, Adhatodine, carotene, Adhavasinone, Anisotine, Vasakin, Vasicinone, Vascicolone, Vasicolinone and moreover ) (https://www.gyanunlimited.com/health/vasaka-malabar-nut-medicinal-uses-benefits-and-side-effects/11317/) (5).

**Respiratory Disorder** (RD) is a common and significant cause of the illness and death around the world. In 2012, Respiratory conditions is the most frequent reasons for the hospital stays patient among children. In Pakistan the acute respiratory infections constitute 30–60% of outdoor patients in hospital including the 80% upper respiratory tract infections and the 20% lower respiratory tract infections. The most common problems of the respiratory system are: asthma, bronchitis, common cold, cough and whooping cough. People are depending on the indigenous of plant resources to the treat various respiratory disorders. Herbal remedies are the treatment of respiratory disorders are common practice in much portions of world. (3)

**Bronchodilator** is the substance they are dilates the bronchi and bronchioles, decreasing the resistance in the respiratory airway and increasing airflow to the lungs. Bronchodilators is endogenous (It is source naturally through the body), or they may be medications administered in treatment of breathing issues. It is most useful in obstructive lung diseases, asthma and chronic obstructive pulmonary disease are the most usual conditions. Although it remains uncertain they might be beneficial in bronchiolitis and bronchiectasis. They are specified but of unproven significance in restrictive lung diseases (3)

**Central cough suppressants**

Chest cold is an important to multitude protection mechanism to clear sputum and strange bodies to from the air passage. The exception of non-physical cough, and cough receptors in the airway are stimulated, the momentum is transmission to the cough center, and then cough is elicited through efferent nerves. Antitussives are classified dependence on, they act in the cough unconscious pathway: middle antitussives act on the cough focus, and peripheral antitussives that act on cough receptors. The agents confidential as peripheral antitussives, especially with regard local anesthetics, expectorants and mouthwashes, it is primarily have to the other effects and broadly classified as the antitussives only since, of their secondary effects on cough receptors. Those classified are more narrowly as antitussives are central cough suppressors.

**Expectorants**

Expectorants is the ancillary antitussives in the general sense, they avoid stimulation of the cough receptors by cleanup sputum from the respiratory. Expectorants are classified established on mechanism of action as mucolytic, mucus-modifying, mucus-lubricant and secretory cell normalizing agents. However, a clear distinction is often difficult. Expectorants have some adverse effects, but thin sputum that is not viscous, the use of mucolytic agents is more difficult to spit. Bronchodilators is the short-acting or long-acting. The Short-acting medications provide to the fast or "rescue" help to acute bronchoconstriction. And the Long-acting bronchodilators assist to control and inhibit the symptoms. It is threesome types of medication Broncho dilating drugs are $\beta_2$ ("beta two")-adrenergic agonists (short- and long-acting), anticholinergic (short-acting), and theophylline (long-acting).

**Short-acting β2-adrenergic agonists**

These are quick-relief medications to that provide quick and impermanent relief from asthma indications or flare-ups. These cures are usually take effect within 20 min. or minimum, and can final

four to six hrs. These inhaled medications are the best for to treating the sudden and severe or new asthma symptoms. Adopted 15 to 20 min. ahead of time, these cures can also to prevent the asthma symptoms by work or revelation to cold air. They are some short-acting β-agonists, such as salbutamol are specific to the lungs and is called $\beta_2$-adrenergic agonists and can relieve bronchospasms without unwanted cardiac side effects of nonspecific β-agonists (ex. ephedrine or epinephrine). Patients are regularly or frequently need to take a short-acting $\beta_2$-adrenergic agonist should consult their doctor, used to indicate uncontrolled asthma, and their routine medications may need adjustment.

**Long-acting β2-adrenergic agonists**

These are long-standing medications adopted routinely in order to the control and prevent bronchoconstriction. It is not purpose for fast relief. These medications may take to longer working, but relieve respiratory airway constriction for up to 12 hours. It is commonly to adopted twice a day with the anti-inflammatory medication, they maintain open airways and prevent asthma symptoms, particularly at the night (3)

**Anticholinergics**

Ex. of anticholinergics are tiotropium (Spiriva) and ipratropium bromide. Tiotropium is the long-acting, 24-hour, and anticholinergic bronchodilator usage in the management of chronic obstructive pulmonary disease (COPD). It is only available as inhalant, and ipratropium bromide is used in the medication of asthma and COPD. They are short-acting anticholinergic, it enhance lung function and decrease the risk of aggravation in people with characteristic of asthma. It will not stop an asthma attack previously in progress. Because it has no effect on asthma indications when used alone, it is the most often paired with a short-acting $\beta_2$-adrenergic agonist to considered a relief or deliver medication, it can take a full hour to the operate. For this reason, it plays a secondary role in acute asthma therapy. Dry pharynx is the most common side effect. If the treatment gets in contact with the eyes, it may produce the blurred vision for a brief time.It is used of anticholinergics in combining with short-acting $\beta_2$-adrenergic agonists has been shown to decrease hospital admissions in children and adults with acute asthma provocations (3).

## MATERIALS AND METHODS

**Collection of Plant Materials and Chemicals**

*Justicia adhatoda* were purchased from the botanical garden in Nashik in Maharashtra, India. Specimen was authentified by the Botanical Survey of India, Western Regional Centre, 7-Koregoan Road, Pune-411001, India. Fresh Leaves were deatached from the plant and then shade dried for 10-14 days under room temperature. After dried leaves is crushed in Commercial electrical stainless-steel blender was used and material was converted into powdered form and saved for further analysis. Prior to analysis, the leaves were ground into powder form. Gelatin, propylene glycol, Methyl paraben, and Propyle paraben were purchased from SD Fine Chem, Mumbai, India. Stevia was procured from Green Valley, Punjab. Colors and Essence were purchased from local confectionary shop. All other ingredients were of analytical grade and procured from registered venders. Double distilled water was used for the experiment. (4)

**Extraction (Soxhlation)**

Plant material (20 g) was extracted with methanol by using Soxhlet extraction method. Crude extracts obtained were evaporated to dryness at 50 ºC and kept in a screwed cap bottle at -18 ºC. All extracts were collected and evaporated at room temperature. (5)

**HPTLC Analysis**

HPTLC chromatogram develop a rapid, efficient and reproducible method of analysis for vasicine. Combination of working standard of vasicine has shown peak in HPTLC chromatogram together with their corresponding UV spectra. HPTLC chromatogram of methanolic extract showed the presence of marker compounds such as vasicine. Optimized condition of Silica gel 60 F254 precoated plates (10 x 10 cm) were used with Dioxane-ammonia (9:1) as solvent system. Test samples were spotted on precoated HPTLC plates. The bandwidth applied on plate was 6 mm and ascending mode was used for development of thin layer chromatography. Saturation time was 25 mins. TLC plates were developed upto 8 cm. The TLC plates were scanned at 254 nm for quantification purpose. Drug sample is *Justicia adhatoda* extract, Detection of sopt in Dragendroff reagent (6)

**Formulation**

The formulation was prepared by the heating and congealing technique using $3^2$ factorial design were applied for the optimization of the process parameters including concentration of gelatin and propylene glycol. The formulation contained *Justicia adhatoda ,* stevia, gelatin, propulene glycol, methyl paraben, propyl paraben, propylene glycol, essence and colors. All the ingredients are weigh acuurately. In one beaker gelatin, propylene glycol were taken and heated to dissolved gelatin with constant stirring. In one container sugar syrup will be set up by including required amount of sugar in measuring beaker and make up the volume up to 100 ml. Completely dissolve the solution, then stabilizer, citric acid add with stirred to enhance softness of the jelly and to maintain pH respectively, then boil for few min. After boiling the above solution, then preservative will be add to the solution, they are mixed thoroughly and uniformly. Now drug is weight precisely and broke up in appropriate vehicle and added before jelly is permitted to set, blend completely.All solution is transferred in to moulds and allowed to cool and settle undisturbed by proper covering the mould's to avoid exposure to outer environment.(7)

**Factorial Design Experiments**

A $3^2$ full factorial design was used in the present study. For factorial design the solvent casting method was selected. In this design 2 factors were evaluated each at 3 levels, and experimental trials were performed at all 9 possible combinations. The amount of Gelatin (X1) and Propylene glycol (X2) were Selected as independent Variables and each factor being studied at -1, 0, +1 level. The dependent variables of viscosity and % extract release were selected on the basis of the preliminary studies carried out before implementing the experimental design. All other formulation and processing variable were kept constant throughout the study. Optimization of prepared Jelly formulations was done by Design Expert Software (Version 11, Stat-Ease Inc., and Minneapolis, MN). All the above formulations were prepared and evaluated for various parameters, and the effects of the Gelatin, Propylene Glycol concentration were studied on the Viscosity and % extract release. Design expert software (Version 11, Stat-Ease Inc., and Minneapolis, MN) was used to treat the data and evaluate the effects. (25) The adequacy of fitted model was checked by the analysis of variance (ANOVA). The main and interaction effects were represented as response surface curves too. Each sample was tested in triplicate for all the experiments. The results of all experiments were expressed as mean±SD. In all tests, values of ($p<0.05$) were regarded as significant. (8-9)

**Characterization of Jelly Formulation**

The prepared *Justicia adhatoda* formulation were evaluated as per the standard procedures reported in the literature.

1. **Physical Appearance:**
   The jelly formulations were analyzed for their physical appearance in terms of clarity, texture and consistency, which are the prime characteristics of a nutraceutical formulation.
2. **Stickiness and grittiness:**

Texture of the medicated jelly in terms of stickiness and grittiness had been evaluated by visual inspection of the product after mildly rubbing the jelly sample between two fingers.

3. **Spreadibility:**
   Spreadibility was determined by apparatus, which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadibility is measured on the basis of 'Slip' and 'Drag' characteristics of jelly. A ground glass slide is fixed on this block. An excess of jelly (about 2gm) under study is placed on this ground slide. The jelly is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. The top plate is then subjected to pull with the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted and weight in gram was recorded(10)
4. **pH:** The pH of all the jelly was determined using digital pH meter. 0.5 gm of the weighed formulation was dispersed in 50 mL of distilled water and the pH were noted. (Indian Pharmacopoeia 2014)
5. **Viscosity:** Viscosity had been measured using Brookfield Viscometer (model LV-DV- II, Helipath-spindle type S-96). As the system is Non- Newtonian spindle no.S-96 were used. (Indian Pharmacopoeia 2014)
6. **% Extract Content:** The content uniformity test is to ensure the every dosage form contains equal amount of extract substance. Jelly from the each formulation were taken, crushed and mixed. From the mixture extract equivalent of mixture was extracted thoroughly with suitable media. The amounts of extract present in each jelly were determined using suitable analytical method. (Indian Pharmacopoeia 2014)
7. ***In-vitro* Dissolution Study:** An in –vitro dissolution study will performed with USP type II paddle apparatus using phosphate buffer 6.8 dissolution medium.(Electro lab dissolution tester) Dissolution medium was kept at 37ºC± 0.5ºC and 100 rpm. The sample is withdrawn after 5, 10, 15, 30, 45, 60 minute and replaced with fresh media. The Samples were determined for extract release using suitable analytical method. (USP 2006)
8. **FTIR Spectroscopy:** To study the compatibility of drug with excipients, IR spectra of drug in combination with excipients in ratio of 1:1 were studied and compared with standard peaks present in the individual monographs in compendial literature. The IR range appeared in Fig.21 shows that there was no physicochemical communication in the middle of medication and the excipients utilized. The characterstics IR absorption region of important bands necessary in the elucidation of drug and excipients presented below. Result of the Preformulation study suggested that all the studied excipients were compatible with *Jasticia adhatoda extract powder*.
9. **Accelerated Stability Studies:** The stability study was evaluated as per ICH guidelines, in the below conditions. (ICH Q1 (R2) guideline) In this study, effect of temperature and humidity was studied by analyzing the optimized batch kept in environmental chamber maintained at temperature like 4°C, $40^0$C± $2^0$C/ 75% ± 5% RH and at room temperature. The stability studies are carried out for 3 months and the formulations were analyzed for the changes in the physical parameters like appearance, pH and % extract content at 15 days, 30 days and 90 days. (Nataranjan R, *et.al,* 2014).

## RESULTS AND DISCUSSIONS

**Preformulation study**

**Plant profile**

- **Name of plant:** *Adulsa ( Vasaka)*
- **Kingdom:** Plantae
- **Botanical name:** *Jasticia adhatoda L.*
- **Family:** Acanthaceae
- **Synonyms:** *Justicia adhatoda Nees*
- **Part of plant:** Leaf
- **Colour of powder:** Grey-Brown
- **Taste:** Bitter

**Physical characteristics of *Justicia adhatoda L.* extract powder [Table No.1]**

| Sr.no | Parameter | Preliminary studies |
|---|---|---|
| 1 | Color | Grey brown |
| 2 | Appearance | brownish crystalline powder |
| 3 | Odour | Characteristic |
| 4 | Taste | Bitter |
| 5 | Loss on drying | 0.10±0.7 |
| 6 | Total Ash | 3.90±0.93 |
| 7 | pH | 6.46±0.052 |

**Melting Point [Table No.2]**

| Sr. No | Temperature ( $^0$C ) |
|---|---|
| 1 | 209 |
| 2 | 211 |
| 3 | 210 |
| Average | 210±0.81 |

The softening purpose of concentrate was observed to be 210, which is consenting to the dissolving point announced (209-2110C).

**Solubility determination of *Justicia adhatoda* [Table No.3]**

| Solution | Solubility |
|---|---|
| Methanol | Soluble |
| Ethanol | Soluble |
| Water | Slightly soluble |

**HPTLC Analysis**

HPTLC chromatogram of methanolic extract showing the presence of two marker compounds such as vasicine and vasicinone along with their respective UV spectra. Standard Vasicine indicated in HPTLC chromatogram. The alignment bend of Vasicine was acquired by spotting standard Vasicine on HPTLC plate. Quantitative estimation proved the presence of biomarker Vasicine in *Jasticia adhatoda* extract. Vasicine and vasicinone are reported to have bronchodialatory and respiratory stimulation effects and hence regarded as biological markers for standardization of *Jasticia adhatoda* extract. Few chromatographic methods are available and reported, such as HPTLC. Peak of UV spectra vasicine show in fig. 18 spectrum of standard vasicine. The Dioxane-ammonia (9:1) solvent system was ideal as a mobile phase that produced $R_f$ 0.4–0.5 for vasicine. The spots were observed at 254 nm and the resultant three-dimensional densitogram configurations of the test samples and

standard vasicine demonstrated that the peaks for all the samples corresponding to $R_f$ 0.5 were overlaying. The features of the corresponding spectrum of this peak were noted to match precisely with each other, revealing the compounds analogous to $R_f$ of the standards. The limitation of reported HPTLC methods are use of ammonia in solvent system, which is hazardous, higher limit of detection & quantification and linear range, which demonstrates lower sensitivity and precision and use of water in mobile phase with lower linear range. HPTLC method was attempted for fast, precise, sensitive and reproducible method with good recoveries for standardization of extracts of *Jasticia adhatoda.*

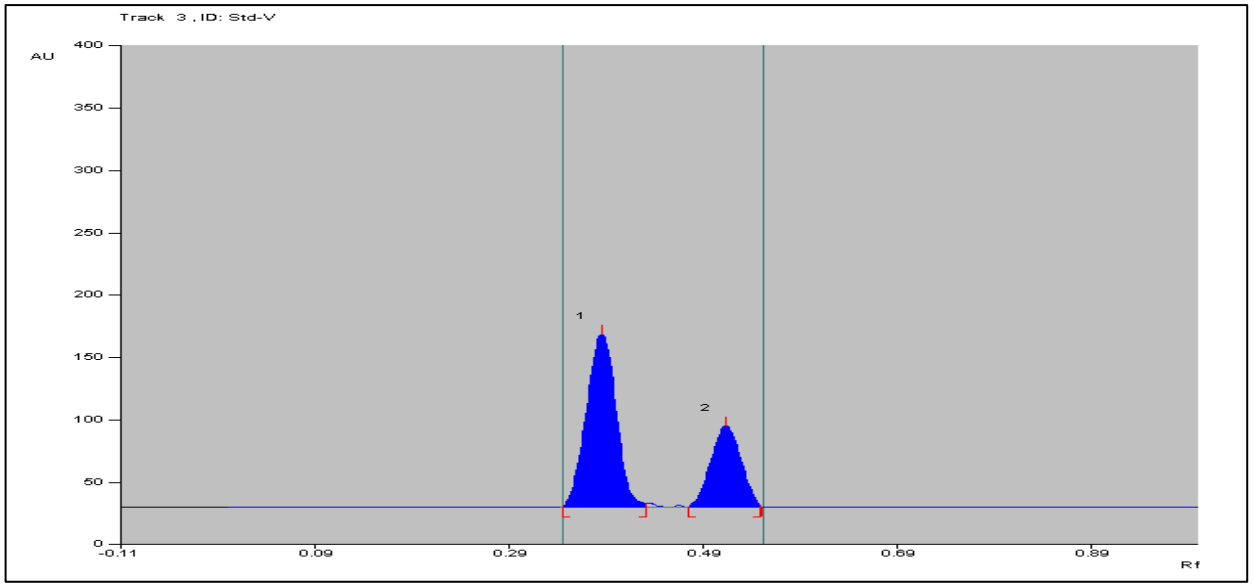


**Figure.2. HPTLC chromatogram of showed standard vasicine mixture**

**(Resolution peak in fingerprinting)**

After improvement the plate was examined at 254 nm, which is appeared in Figure.21. Quantitative estimation proved the presence of biomarker Vasicine in *Jasticia adhatoda* extract. Vasicine and vasicinone are reported to have bronchodialatory and respiratory stimulation effects and hence regarded as biological markers for standardization of *Jasticia adhatoda* extract. Few chromatographic methods are available and reported, such as HPTLC.

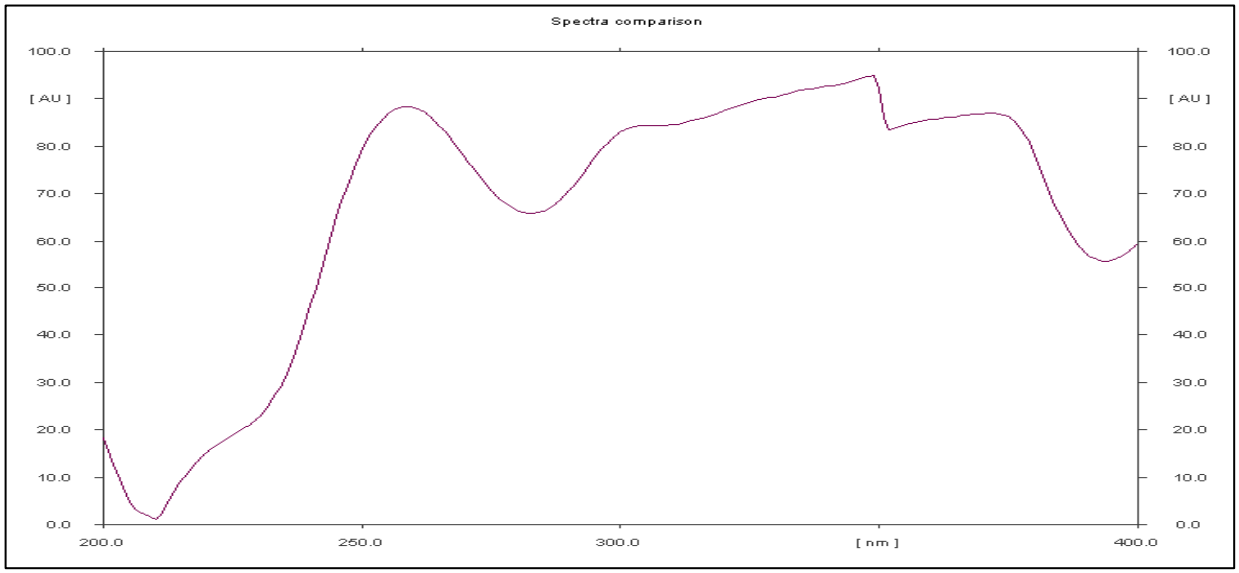


**Figure.3. Spectrum of standard vasicine**

Peak of UV spectra vasicine show in fig. 18 spectrum of standard vasicine. The Dioxane-ammonia (9:1) solvent system was ideal as a mobile phase that produced $R_f$ 0.4–0.5 for vasicine.

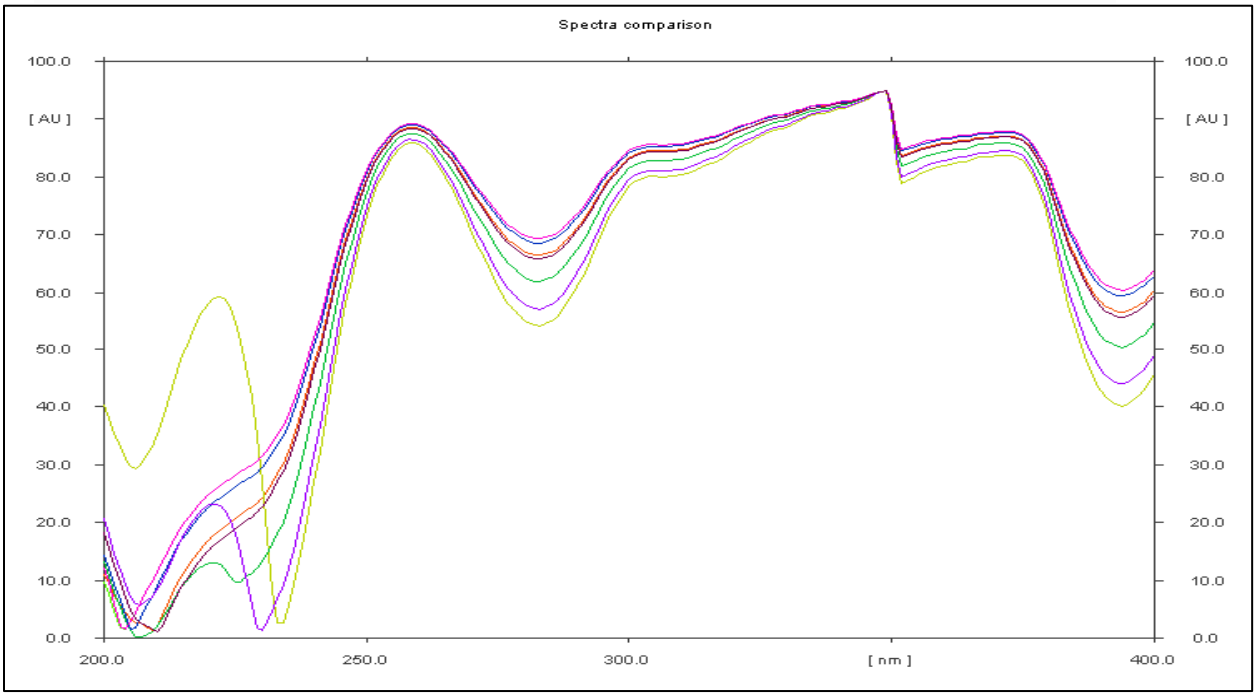


**Figure.4. Overlay spectra of standard vasicine**

The spots were observed at 254 nm and the resultant three-dimensional densitogram configurations of the test samples and standard vasicine demonstrated that the peaks for all the samples corresponding to $R_f$ 0.5 were overlaying. The features of the corresponding spectrum of this peak were noted to match precisely with each other, revealing the compounds analogous to $R_f$ of the standards.

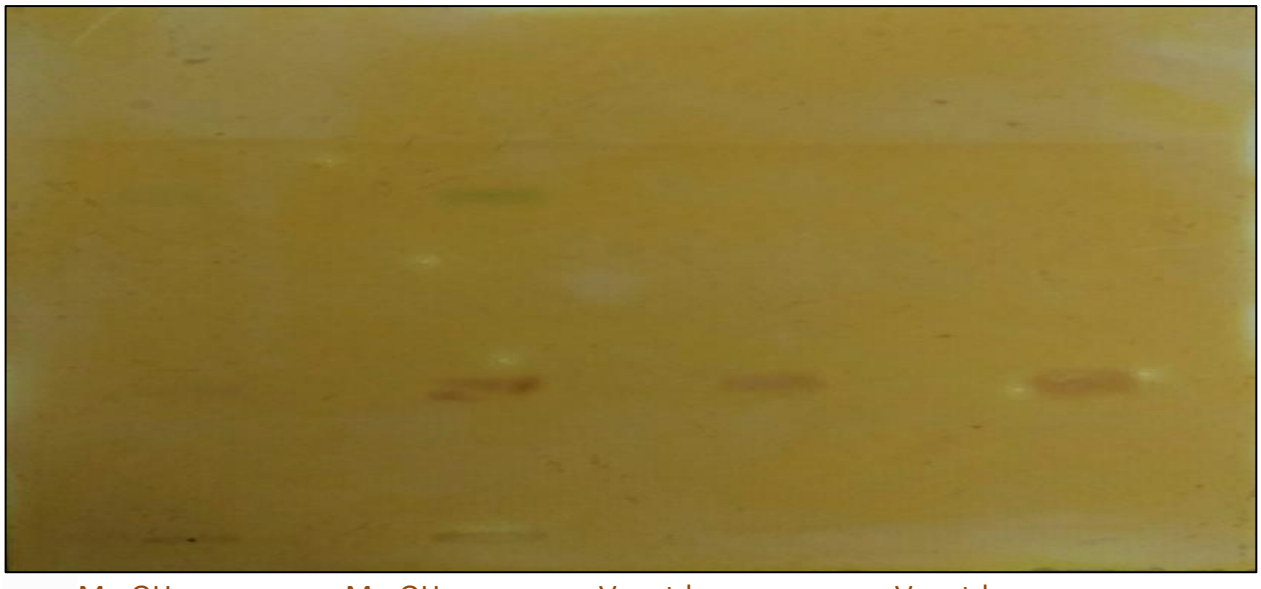


**Figure.5. Fingerprinting derivetization**

The limitation of reported HPTLC methods are use of ammonia in solvent system, which is hazardous, higher limit of detection & quantification and linear range, which demonstrates lower sensitivity and

precision and use of water in mobile phase with lower linear range. HPTLC method was attempted for fast, precise, sensitive and reproducible method with good recoveries for standardization of extracts of *Jasticia adhatoda*

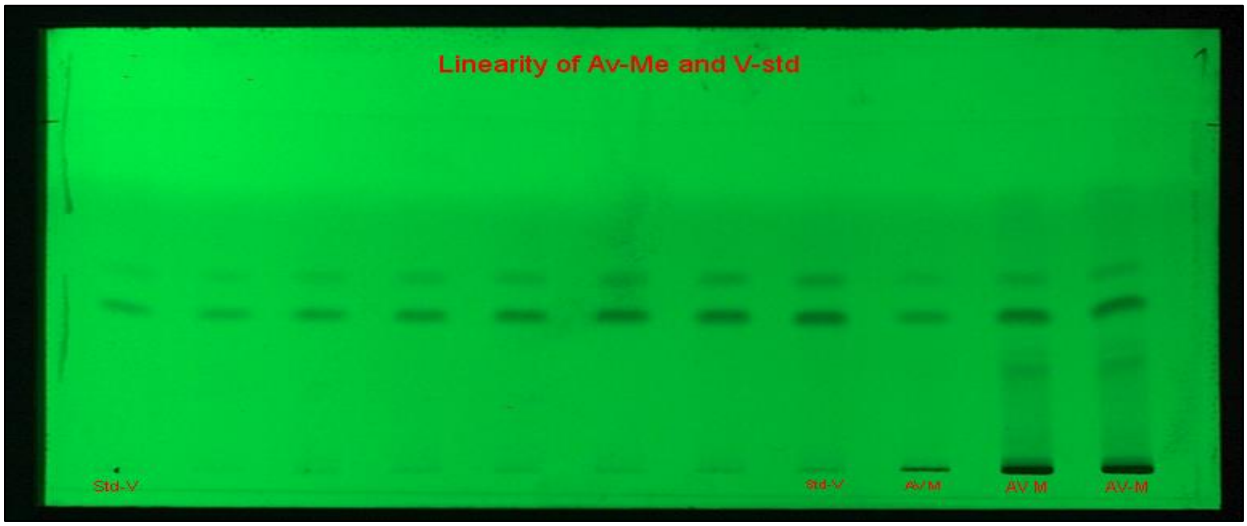


**Figure.6. TLC plate showing the distinct separation of vasicine after development (Fingerprinting at 254nm)**

In the present study preliminary Qualitative phytochemical screening was identified and confirmed the major alkaloid vasicine present in plant extract.The quantitative estimation and confirmation vasicine was done after comparing the color of the zone with the colour of the reference compounds. Spots were observed in short wave UV 254 nm and five spots in long wave uv 366 nm.

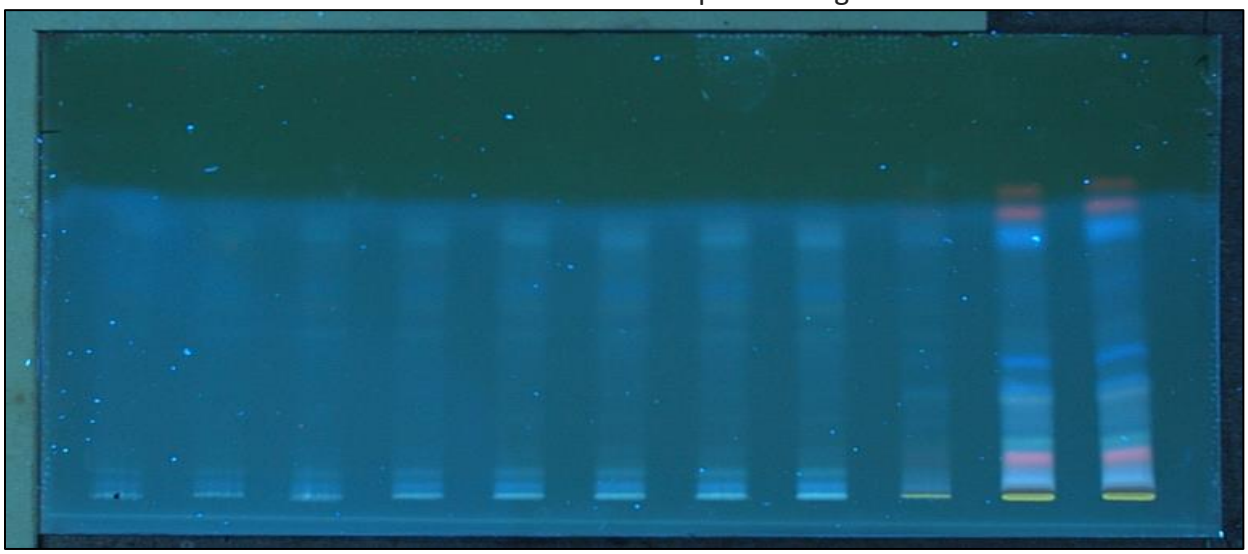

**Figure.6. Fingerprinting at 366nm**

The spectrum of standard compound Vasicine and the corresponding spot present in leaves of *Jasticia adhatoda matched* exactly, indicating no interference by the other plant constituents and excipients. Visual observation under UV light showed few spots, but on analyzing under densitometer much more was observed.

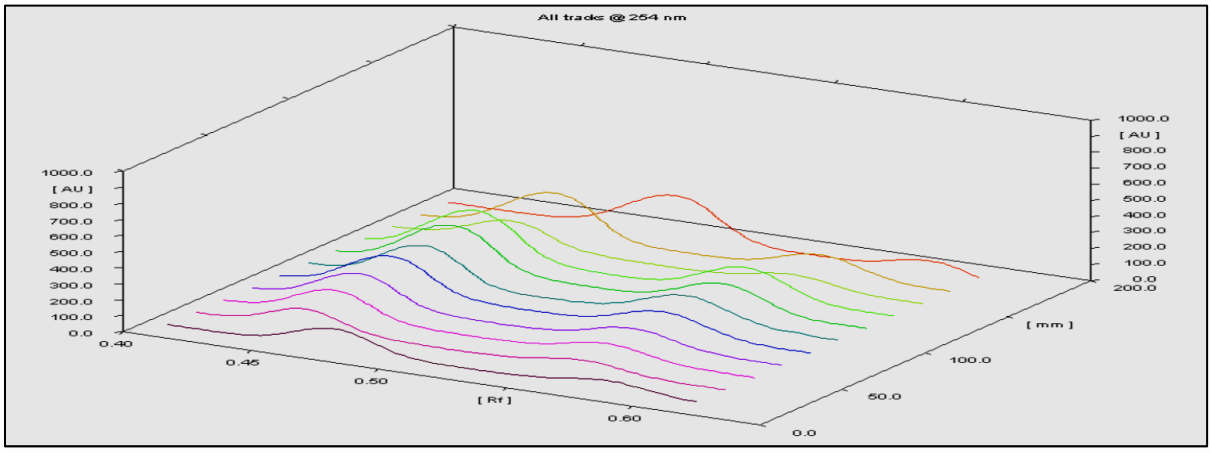


**Figure.7. 3D Graph of Linearity**

The linearity calibration curve was found between 2 and 6 µg/spot with a respective correlation coefficient. 3D graph of linearity show all tracks at 254nm and 366nm. HPTLC analysis was colored zone of bright orange spoken to the nearness of alkaloids which was identified in the present study.

**Linearity (Table no. 4)**

| Sr. No. | Conc. (ng) | AUC | | | Average AUC | SD | % RSD |
|---|---|---|---|---|---|---|---|
| | | Area I | Area II | Area III | | | |
| 1 | 200 | 1341.8 | 1376.3 | 1301.4 | 1339.8 | | |
| 2 | 300 | 2568.9 | 2504.3 | 2553.9 | 2542.3 | | |
| 3 | 400 | 3996.5 | 5707.4 | 3996.8 | 3990.0 | 11.40 | 0.28 |
| 4 | 500 | 5553.9 | 5707.4 | 5408.0 | 5489.7 | | |
| 5 | 600 | 6479.8 | 6662.1 | 6541.2 | 6561.0 | | |

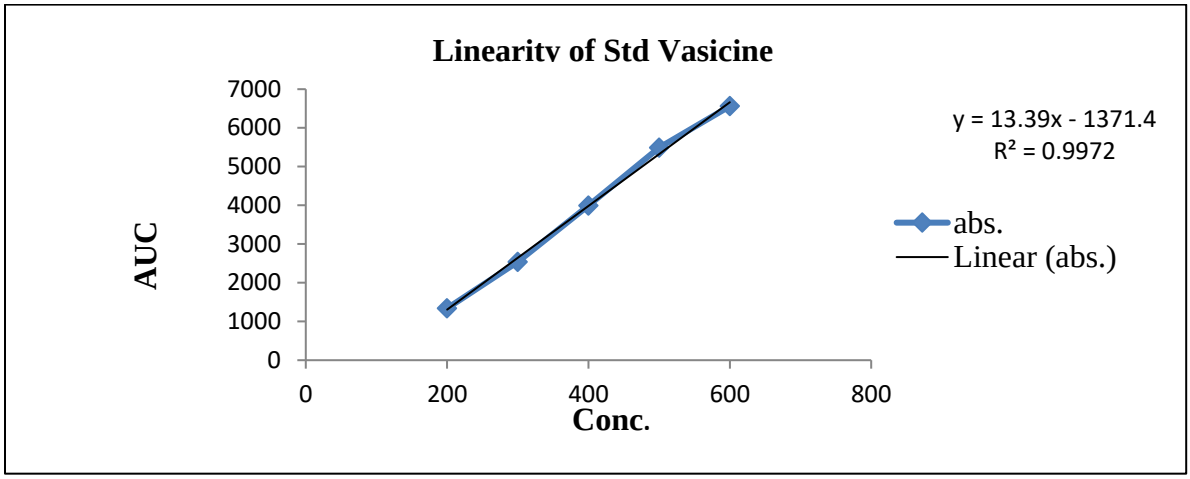


**Figure.8. Lenearity of Std Vasicine**

**Statistical Analysis**

Statistical investigation covers a lot of analyses and makes certain exact and powerful elucidation of consequences of an examination which decide the reaction factors, leading proper statistical tests to choose most ideal model fitting scientific models to the information and deciding the estimations of free plan factors to deliver ideal reaction. The present examination connected a factorial structure which is one of the prominent factual test configurations to streamline the plan just as to find the communication, if any between the variables picked. To study the effects of independent variables on its attributes and performance, a $3^2$ full factorial design was applied. The independent variables such as concentration of gelatin and concentration of propylene glycol at two levels were evaluated for their effect on viscosity and % extract release. The estimation of explored reactions estimated for all preliminary definitions were fitted in the $3^2$ factorial outlines to get display conditions for reactions analyzed in this examination. These models were evaluated statistically by applying one-way ANOVA ($p< 0.05$). All the responces studied were largely affected by the variables chosen as reflected from the results of regression analysis and ANOVA. The viscosity of jelly wasfound in the range of 3200-4200ps. The result of regression analysis indicated that the viscosity from the formulation was significantly affected by the variables of the study ($r^2 = 0.9243$). A comparison of the predominant effect of the gelatin and propylene glycol concentration both are positive indicating that both have direct realtion with the viscosity. The response surface curve generated out of the results pointed out with increase in jelly viscosity due to the concentration of excipients increases. It was observed that higher concentration of excipients increses the viscosity. The regression equation for viscosity was:

Viscosity= - +2456.00000+1440.66667*A. +503.16667*B. ($r^2 = 0.9243$, Fvalue =33.21,$p< 0.05$,i.e.,)

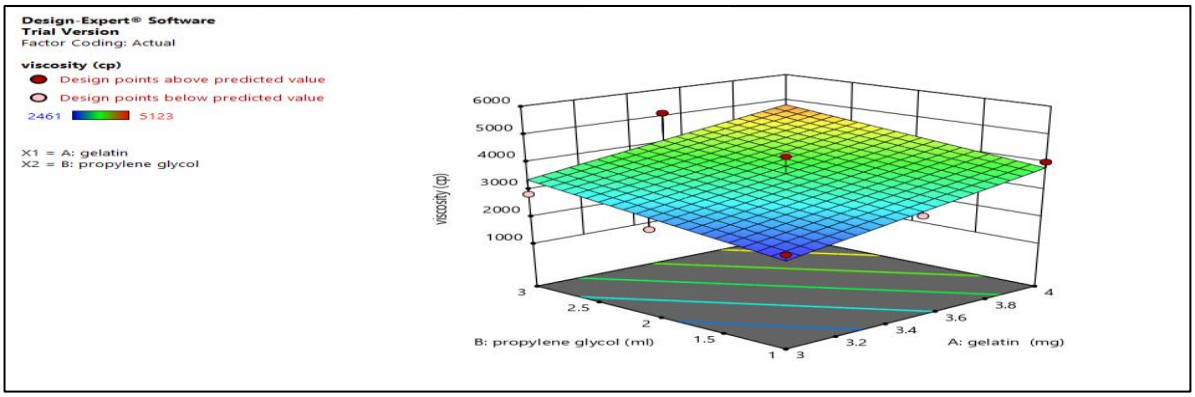


**Figure.8. 3D Response Surface Plot showing the influence of Gelatin, Propylene glycol on the Viscosity of jelly.**

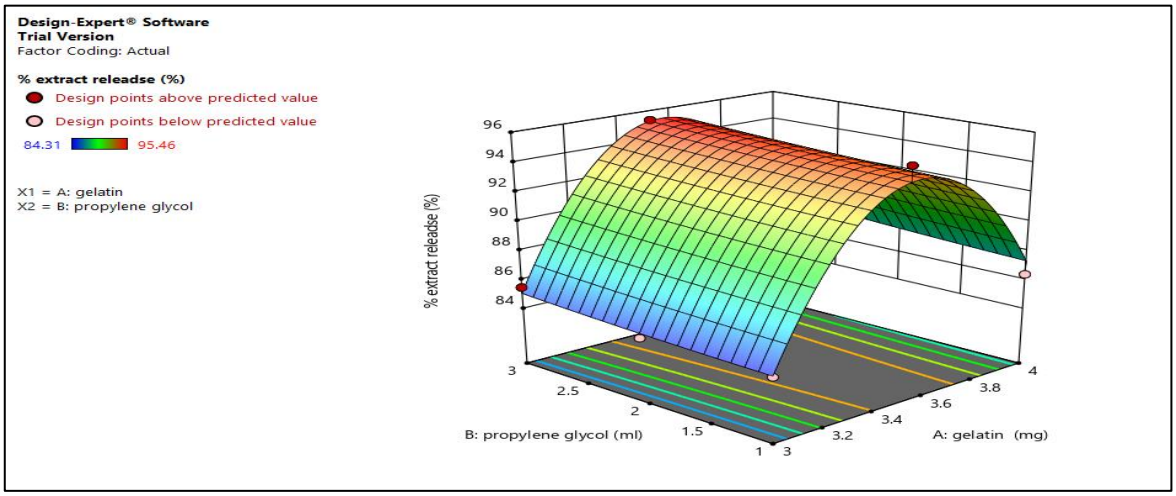


**Figure 9. 3D Response Surface Plot showing the influence of Gelatin, Propylene glycol on the % extract release of jelly.**

% extract release = -333.56722+241.75000*A.-0.680833*B. +0215000AB.-34.14667$A^2$+0.088333 $B^2$ ($r^2$ = 0.9215, F value = 21.12, $p < 0.05$, i.e, significant)

In this equation shows the positive sign of the coefficient indicated a synergistic effect while a negative sign indicated an antagonistic effect on the response. The larger coefficient means the independent variable has more potent influence on the response

**(Table no. 5) Optimization Batches Obtained After Applying $3^2$ Factorial Desighn In Actual Values**

| **Ingredients (%)** | **Batch** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| *Justicia adhatoda* Extract (g) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Gelatin (g) | 0.15 | 0.17 | 0.15 | 0.2 | 0.15 | 0.17 | 0.17 | 0.2 | 0.2 |
| Propylene Glycol (ml) | 3 | 3 | 1 | 3 | 2 | 2 | 1 | 1 | 2 |
| Stevia (g) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Methyl paraben (g) | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| Propyl paraben (g) | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| Colouring agent | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| Flavouring agent | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| Water | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |

**Evaluation of Jelly**

**12.1 Physical Appearance**

The physical entrance of F1-F9 batches of *Jasticia adhatoda* jellies was studied. All the batches owned a smooth texture and a continuous homogenous nature. Although, the formulations appeared turbid in common appearance, quite opposing features than that of marketed products which are always translucent or transparent. (Table no. 6.)

| Formulation code | Clarity | Texture | Consistency |
|---|---|---|---|
| F1 | Turbid form | Smooth | Thin |
| F2 | Turbid form | Smooth | Thick |
| F3 | Turbid form | Smooth | Fluid like |
| F4 | Turbid form | Smooth | Very Thick |
| F5 | Turbid form | Smooth | Thin |
| F6 | Turbid form | Smooth | Thick |
| F7 | Turbid form | Smooth | Fluid like |
| F8 | Turbid form | Smooth | Thin |
| F9 | Turbid form | Smooth | Thin |

**Stickiness and grittiness**

The formulation F3 to F7 showed high stickiness, formulation F1, F5, F8 to F9 displayed less stickiness properties, whereas the formulation F2, F4 to F6 exhibited no such stickiness. It can be terminated that as the concentration of gelatin and propylene glycol was inhance to get the stickiness, grittiness gets reduced for jelly. The stickiness and grittiness of F1-F9 batches of corn silk jellies was considered. (Table no. 7)

| Formulation code | Stickiness | Grittiness |
|---|---|---|
| F1 | Less sticky | Less gritty |
| F2 | Non-sticky | Slightlygritty |
| F3 | Sticky | Gritty |
| F4 | Non-sticky | Slightlygritty |
| F5 | Less sticky | Less gritty |
| F6 | Non-sticky | Slightly gritty |
| F7 | Sticky | Gritty |
| F8 | Less sticky | Less gritty |
| F9 | Less sticky | Less gritty |

**Spreadibility**

The spreadibility of F1-F9 batches of *Jasticia adhatoda* jellies was considered. It can be conclude that inhance the concentration of propylene glycol to get inhance the slickness of the jelly. The results for spreadability was shown in the Table. 23

**pH**

The pH of formulations was measured to be in the range of 6.02 to 7.11. Formulation F6, the optimized formulation, showed pH of 6.63 which is nearest to neutrality. The pH of F1-F9 batches of *Jasticia adhatoda* jellies was considered. The results for pH was shown in Table no. 23

**Viscosity**

The viscosity was observed in the range of 3200–4200 ps. It can be concluded that as the concentration of gelatin was increased from 3% to 4% and the concentration of propylene glycol was increased from 1% to 3% the viscosity increased concurrently. The combining of the gelatin and propylene glycol played an important role in maintaining the consistency of the formulations. The

Viscosity of F1-F9 batch of *Justicia adhatoda* jellies was considered. The results for Viscosity was shown in the Table no. 23

**% Extract Content**

The extract content in formulations was observed in the range of 88.62–95.81%. The higher drug content of 95.81% was determined in formulation F6. The % extract Content of F1-F9 batch of *Justicia adhatoda* jellies was considered. The results for % extract Content was shown in the Table no. 23

**[Table No. 8]**

| Batch code | Spread ability (gm.cm/Sec) | pH | Viscosity (cp) | Drug content (%) |
|---|---|---|---|---|
| F1 | 26.05±0.71 | 7.11±0.09 | 2561±32.34 | 88.62±0.82 |
| F2 | 31±0.32 | 6.77±0.06 | 4021±30.60 | 93.23±0.62 |
| F3 | 22.74±0.73 | 6.60±0.08 | 2845±92.34 | 86.47±0.03 |
| F4 | 31±0.90 | 6.31±0.15 | 2461±93.30 | 94.74±0.51 |
| F5 | 23.05±0.24 | 7.07±0.02 | 2935±40.88 | 91.22±0.02 |
| F6 | 26.06±0.73 | 6.63±0.12 | 4568±52.38 | 95.81±0.27 |
| F7 | 25.53±0.46 | 6.02±0.08 | 3600±06.24 | 94.89±0.20 |
| F8 | 23.16±0.34 | 6.93±0.07 | 4220±23.76 | 93.23±0.07 |
| F9 | 27.07±0.89 | 6.20±0.15 | 5123±16.11 | 94.25±0.57 |

***In-vitro* Dissolution Study**

**[Table No. 9]**

Percentage cumulative extract release of batches F1 to F9

| Time (min) | %Cumulative Extract Release (Mean±S.D.)* | | | |
|---|---|---|---|---|
| | F1 | F2 | F3 | F4 |
| 5 | 61.07±0.34 | 56.74±0.096 | 70.25±4.46 | 55.56±0.31 |
| 10 | 68.66±0.42 | 60.95±0.091 | 73.47±0.32 | 60.76 ±0.38 |
| 15 | 72.23±0.14 | 68.18±0.033 | 80.71±0.62 | 63.58±0.17 |
| 30 | 78.92±0.095 | 73.76±0.056 | 82.99±0.41 | 69.34±0.26 |
| 45 | 83.97±0.35 | 79.72±0.019 | 86.38±0.81 | 76.77±0.096 |
| 60 | 84.34±0.14 | 82.39±0.33 | 85.46±0.46 | 84.31 ±0.36 |

| Time (min) | %Cumulative extract Release (Mean±S.D.)* | | | | |
|---|---|---|---|---|---|
| | F5 | F6 | F7 | F8 | F9 |
| 5 | 70.69±0.26 | 68.41±0.084 | 68.05±0.062 | 66.76±0.005 | 67.13±0.22 |
| 10 | 73.62±0.07 | 75.47±0.026 | 70.88±0.032 | 70.19±0.021 | 72.34±0.71 |
| 15 | 79.12±0.74 | 86.21±0.40 | 74.08±0.073 | 72.32±0.042 | 75.45±0.051 |
| 30 | 84.82±0.72 | 90.89±0.62 | 82.42±0.29 | 79.99±0.32 | 80.85±0.23 |
| 45 | 88.77±0.22 | 93.56±0.32 | 87.65±0.21 | 85.74±0.81 | 85.18±0.31 |
| 60 | 95.46±0.38 | 96.94±0.11 | 89.24.±0.054 | 93.65±0.07 | 95.34±0.019 |

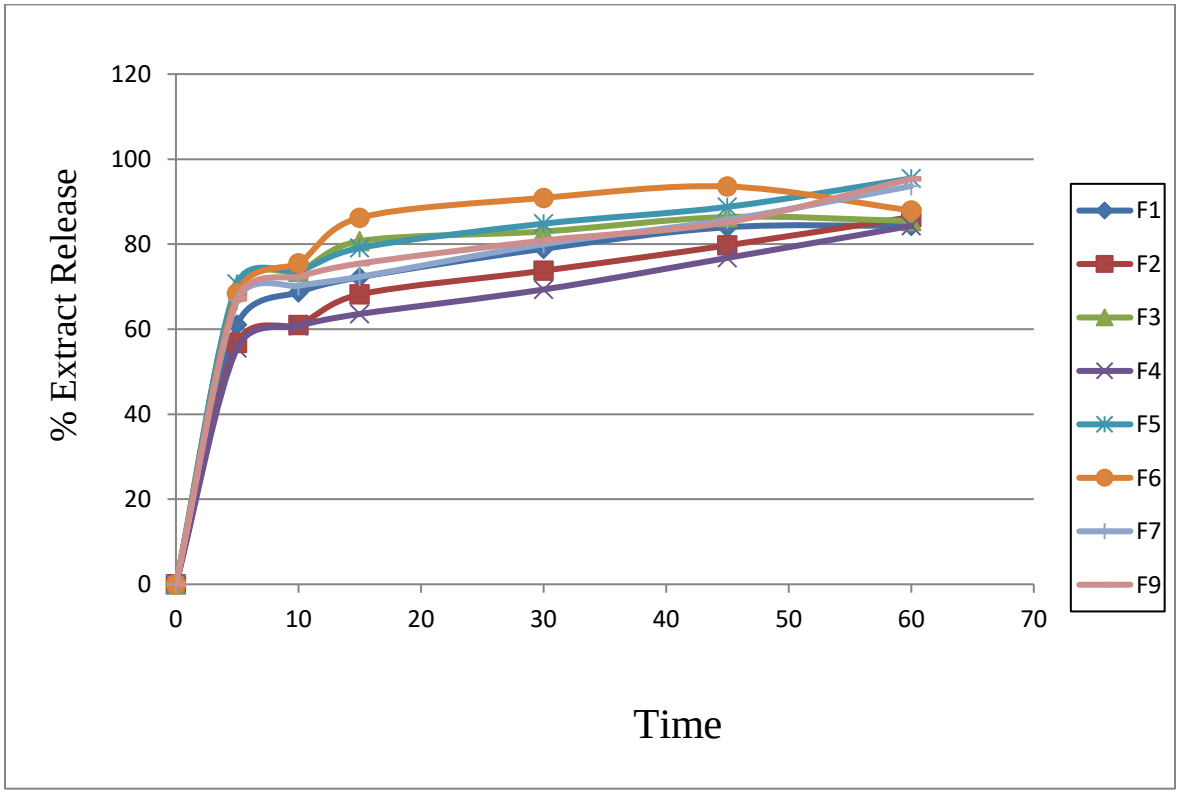


**Figure.25. % cumulative extract release graph of batches F1 toF9**

The in-vitro drug release profiles of formulations (F1 to F9) was considered. All formulations showed different levels of drug release, ranging from 82.39% - 96.94%. It has been observed that as the higher % extract release on F6 batch that the concentration of gelatin and propylene glycol as 3.5% and 2 %.

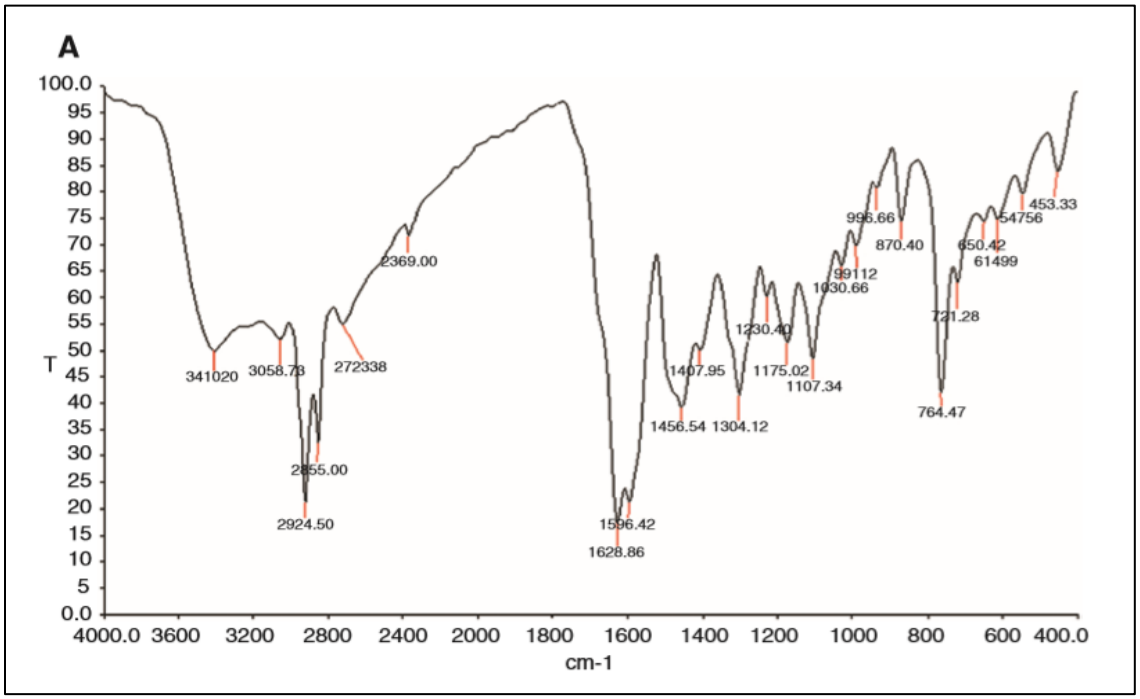


**Figure.12. FTIR of Standard Vasicine**

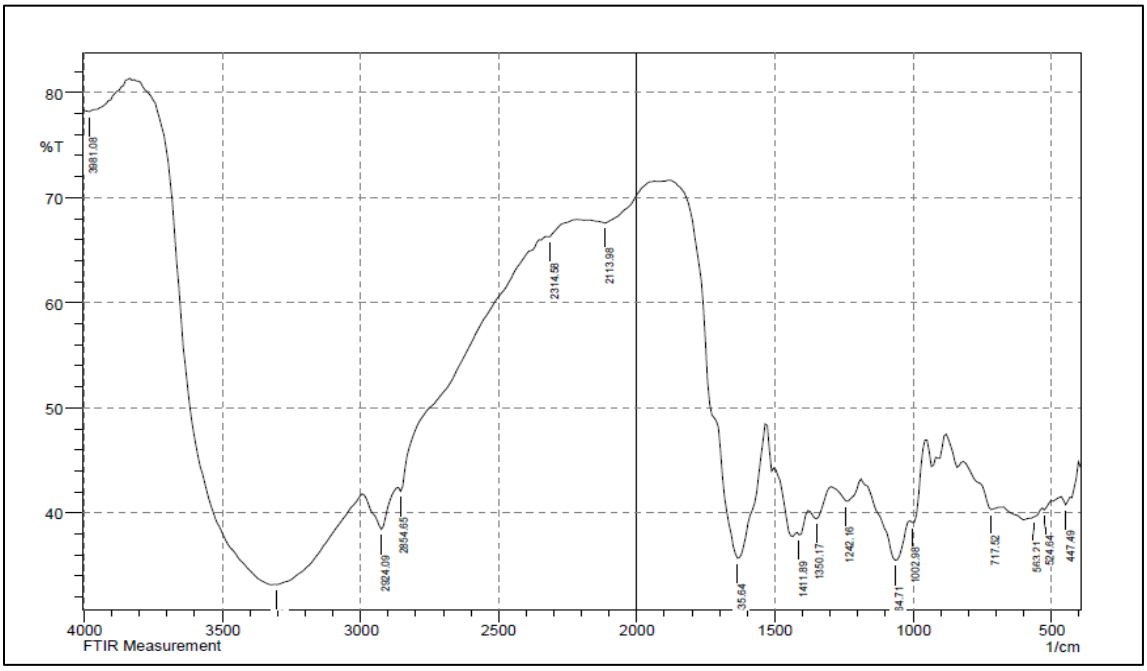


**Figure.13. FTIR of *Justicia adhatoda* Extract**

The principle absorption peak of drug showed O-H stretching hydroxyl group (alcohol) group at 3410 at that frequency and C-H stretching (Alkane) group at 2924, C-O stretching (Ketone) group at 1628, C-N stretching (Amine) group at 1304 at that frequency. Absorption peak of drug showed O-H stretching hydroxyl group (alcohol) group at 3302 at that frequency and C-H stretching (Alkane) group at 2924, C-O stretching (Ketone) group at 1635, C-N stretching (Amine) group at 1350 at that frequency.

**Selection of optimized batch:**

Six solutions were obtained from the design expert software after submitting the optimization data, from which one batch was selected for final scrutinizing of the optimized formula. The optimized batch was evaluated for all the parameters such as Viscosity, pH, % extract content, Spredability, % extract release.

**The Predicted and Actual Values for all Responses** [Table No. 32]

| Batch | Predicted % Viscosity | Actual % drug Viscosity | Predicted % Extract Release | Actual% Extract Release |
|---|---|---|---|---|
| **Optimized batch** | 3920..44 | 3808±34.22 | 93.1092 | 92.51±0.921 |

**Physical Appearance [Table No. 33]**

| Formulation code | Clarity | Texture | Consistency |
|---|---|---|---|
| F1 | Turbid form | Smooth | Thin |

**Viscosity** [Table No. 34]

| Formulation | Viscosity (cp) |
|---|---|
| **Optimized batch** | 3808±34.22 |

**13.7 Spredability** [Table No. 35]

| Formulation | Spredability (gm.cm/sec) |
|---|---|
| **Optimized batch** | 28.30±0.31 |

**13.8 % Extract Content [Table No. 36]**

| Formulation code | % Extract Content |
|---|---|
| **Optimized batch** | 97.90±0.76 |

**13.9 % Extract release [Table No.37]**

| Time in min | Drug release (%) |
|---|---|
| **5** | 68.22±0.473 |
| **10** | 73.13±0.214 |
| **15** | 76.91±0.524 |
| **30** | 82.12±0.101 |
| **45** | 90.09±0.206 |
| **60** | 94.16±0.316 |

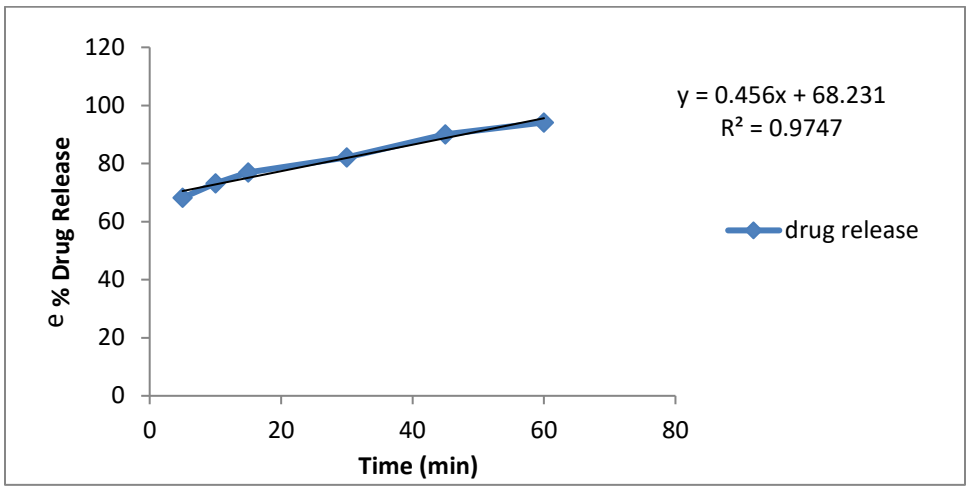


**Figure.33.** Graphical presentation of % Extract Release profile of optimized batch

**Stability Study of jelly**

| **Parameter** | **15 Day** | **30 Day** | **90 Day** |
|---|---|---|---|
| Texture | Smooth | Smooth | Smooth |
| Consistency | Thick | Thick | Thin |
| Stickiness | Non-sticky | Non-sticky | Non-sticky |
| Grittiness | Less gritty | Less gritty | Less gritty |
| pH | 6.3±0.11 | 6.03 ± 0.022 | 6.30± 0.32 |
| Drug Content (%) | 95.91±0.41 | 95.21±0.62 | 95.55± 0.50 |
| % Drug Release | 93.62±0.92 | 92.72±0.65 | 92.01± 0.10 |

The stability study results of optimized formulation are shown in the table. They are optimized formulation were stable and they are accelerated condition of temperature and moisture at ($40^0$C± $2^0$C/ 75% ± 5% RH) for a period of 3 months. The pharmaceutical optimized formulation was recoreded as all properties at day 0, 45, and 90 day. Cover the jelly using aluminium foil and kept in bottle (plastic) for the duration of 3 months.and the jelly was further test it was no important modification of texture, consistency, stickiness, grittiness, pH, % extract content and % extract release on storage at the corresponding conditions. It is similar result in 3 months of stability condition as per ICH guideline.

## CONCLUSION

The present work describes an innovation that *Jasticia adhatoda* product conataing jelly-based formulation. *Jasticia adhatoda* contains more amounts of active constituents which are responsible for the main pharmacological activities like bronchodilator, anti-oxidant, anti-inflammatory, sedative and bronchial antiseptic. The formulation was prepared by the heating and Congealing Technique

using $3^2$ full factorial designs were applied for the optimization of the process parameters including Concentration of gelatine and propylene glycol. Formulation which comprises of *Jasticia adhatoda* extract, gelatine, propylene glycol, methyl paraben, propyl paraben, along with essence and colours. Stevia was used as sweetener which is calorie free and also prevents tooth decay. Prepared formulations observed being stable throughout the stability conditions provided.

The current study highlighted an approach in developing *Jasticia adhatoda based* jelly formulation that will provide a chance to patients in reduces Respiratory disorders, Appropriate controlled oral preparations is necessary for treatment of respiratory problems**,** this is patient-friendly formulation of various age group. The extract, which are used in the dosage form are safe for consumption and can be swallowed without any risk of systemic side effects. Patients can use the developed formulation without hesitation of taste. Being of natural origin negligible side effect. Formulation mostly acceptable by peadiratic and geriatric patient.

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