

Preparation and evaluation of nutraceutical gummies using *Justicia adhatoda* (Vasaka)

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ABSTRACT:As the increased reporting of pulmonary complications due to genetics as well as environmental and lifestyle conditions, the use of respiratory medications were increased tremendously. The most important aspects of these medication for pulmonary complications were, most of the medicines should have to be used by the patient for their entire life. This causes drug dependence and delayed side effects, especially in children. So considering the above mentioned aspects of synthetic medications in our research project aims for the enhancement of pulmonary functions and as a supporting therapy for pulmonary diseases, and it will provide bronchodilation and anti-inflammatory effects in the respiratory tract. Our nutraceutical supplement will prevent and reduce the symptoms of various pulmonary complications and enhance pulmonary functions. As we formulate our nutraceutical product in an oral gummy, it is more acceptable to all age groups, especially children who avoid taking medications can be reduced to a large extent. We have incorporated the leaf extract of *Justicia adhatoda*, extracts of *Zingiber officinale* and *Piper longum* into the gelatin base having sugar syrup. Determination of extractive value, chemical test of alkaloid, TLC analysis of extracts was performed and identified. The prepared nutraceutical gummies were found to be in the stipulated pH range, texture, and it have cough suppressant activity, throat smoothening effect and good solubility parameters. Our nutraceutical gummies were considered sustaining and productive way to enhance pulmonary functions. The prepared formulation was physio-chemically and microbiologically stable, possess characteristics of a standard pharmaceutical formulations. It possesses all the necessary characteristics. features of gummies in the entire period of stability study.

KEYWORDS:Nutraceuticals, Herbal medicine, Oral gummies, Pulmonary enhancer, Vasaka, Natural, Supplements, Plant derived, Bronchodilation, Traditional medicine.

I. INTRODUCTION

A nutraceutical is an alternative to medication that has physiological benefits. The foundation of nutraceuticals is prevention; as the father of medicine, Hippocrates, once said, "Let food be your medicine." Jellies or Gummies are clear or semi-transparent, oil-free, semisolid preparations that can be used internally or externally. Water-soluble bases, such as tragacanth, gelatin, pectin, alginate, and boro glycerin, are the source of oral gummies. In addition, this preparation looks good, which makes it more practical for both young patients and senior people. Additionally, patients with dysphagia and those in the geriatric and pediatric populations accept oral gummies. They can be used in the mouth cavity for both local and systemic therapy. Oral gummies facilitate rapid breakdown of drugs by employing saliva without the need for water and rapid drug absorption through the buccal mucosa, limiting the first-pass effect. Therefore, it provides a substantially earlier onset of action and more effective drug absorption than the tablets that are currently on the market.^[1]

Herbal medicines and herbal supplements have a trend in the market to be known for their limited adverse effects and traditional uses. So here, traditional medicines for common pulmonary complications such as asthma, cough, and shortness of breath are utilized in this formulation. *Justicia adhatoda* also known as Vasaka, is the main ingredient in traditional medicines for respiratory disorders. Vasaka is known as Adalodakam in Kerala, and it is a common household remedy plant for many diseases. *Zingiber officinale*, also known as ginger, is a common kitchen ingredient in Indian

households. It has several medicinal properties and is used widely in a variety of ways, even in dishes. *Piper longum*, also known as long pepper, commonly known as Tippali, has several medicinal properties which can modify the pulmonary functions.

Nowadays, pulmonary complications are common in urban areas. The root cause of the problem was either genetic or environmental. Other than that, some respiratory issues can be caused by lifestyle and occupational conditions. The majority of the urban population suffers from lifestyle diseases. The living conditions and environment around them play an important role in forming a healthy life around them. As we all know, respiratory functions should be good in most cases where they live in a peaceful and pollution-free environment. But as part of urbanization and living culture, people are dedicated to living and suffering in polluted areas. Especially in the case of children, they don't have any choice, but they need to live with their own parents, even if they live in a polluted or non-polluted area. This has caused the rapid rise in respiratory disorders in the past few years. Not only people in urban areas are affected, but also those who are living in rural areas also have pulmonary complications, which are caused by genetic or climatic conditions. Proper health care wasn't delivered in rural areas in underdeveloped countries as well as in developing countries.

Giving an account of the recent pandemic where every corner of the world was affected by 'The COVID-19', the normal functionality of human life has dramatically changed in the past 4 years. In light of that fact, respiratory specialists all across the world have accepted the reduction in lung capacity of humans who are infected by the Corona virus. So if the pulmonary function of the entire population of the world isn't in good condition, we initiate our formulation for enhancing those conditions and providing better care. In India, over 100 million people are suffering from respiratory disorders, and about 1 million patients are dying a year due to asthma and COPD. This may be due to a lack of health monitoring or medication adherence.

The complexity of respiratory medications such as nebulizers, rotahalers, and inhalers can cause medication adherence in patients. And also, the price of respiratory medicines also plays a role in medication adherence. The illiteracy of the patients limits the use of the complex drug administration. Children usually have the tendency to skip some doses due to laziness and craziness, and sometimes children avoid oral medications due to unpleasant taste and smell. Some show difficulty

swallowing medications, which in turn also affects the treatment procedure negatively. Here we are providing a complete remedy for those problems we mentioned above, as we are providing a healthy supplement in the form of gummies. Which is sweet and flavored with natural fruits, and most importantly, they are medicated for a better life.

II. PLANT PROFILE

Justicia adhatoda / *Adhatoda vasica* Linn (fam: Acanthaceae) is commonly known as Vasaka or Arusha. It is a well-known herb in the Ayurveda system for its medicinal advantages. In India, Vasaka was called the Malabar nut tree. For centuries, vasaka has been used for the treatment of various pulmonary conditions, such as asthma, chronic bronchitis, and other respiratory disorders. The use of vasaka leaves in the Ayurvedic system of medicine dates back to 2000 years. Vasicine, the main bronchodilator alkaloid present in vasaka, made it much more popular in traditional medicines. The leaves of the plant are mostly used in medicinal preparations, even though all parts of the plant have medicinal values. This plant is perennial, evergreen, and highly branched, with an unpleasant odor and bitter taste. It also lives for all seasons and retains its leaves throughout the year.

Justicia adhatoda has several medicinal activities that make this herbal plant much in demand, such as anti-inflammatory, antioxidant, antispasmodic, analgesic, hepatoprotective, antimicrobial, antihelmintic, antiulcer, expectorant, dysentery, sedative, diarrhea, antibacterial, antidiabetic, antihistaminic, wound healing, uterotonic, hypotensive, cardiac depressant, and thrombopoietic activity. The leaf extracts of *Adhatoda* are used in the treatment of asthma and chronic bronchitis. It relieves coughing and breathlessness.

The principle constituents of vasaka are the several alkaloids present, the chief of which are quinazoline alkaloids, vasicine, and vasicinone, which are responsible for the bronchodilation and antihistaminic effects. These alkaloids exist in combination with an acid, which is called adathodic acid. The leaves of the plant are rich in vitamin C and carotene and yield an essential oil. By comparing the two major species of vasaka, *Adhatoda vasica* and *Adhatoda beddomei*, *Adhatoda vasica* has a higher concentration of vasicine.^[2]

Zingiber officinale (fam: Zingiberaceae) is an herbaceous perennial, the rhizomes of which are used as spice. It has been commonly consumed as a

spice and herbal medicine since ages ago. Ginger is used to attenuate and treat several common diseases, such as headache, cough, cold, nausea, emesis, gastric obstruction, and so on. In recent studies, ginger has been found to possess several biological activities, such as anti-inflammatory, antioxidant, antimicrobial, and anticancer activities. In addition, studies also open up the various medicinal applications of ginger, showing that it possesses the potential to prevent and manage several diseases, such as respiratory disorders for all ages, neurodegenerative diseases, cardiovascular diseases, obesity, diabetic mellitus, chemotherapy-induced nausea, and emesis.

Many bioactive compounds in ginger have been identified, such as phenolic and terpene compounds. The phenolic compounds are mainly gingerols, shogaols, and paradols. These phenolic ginger constituents have exhibited bronchi dilating activities and antihypertensive activities in several studies that have been conducted by several scholars. It has been proven that ginger can induce significant and rapid relaxation in the isolated human airway smooth muscles. Also, it can reduce allergic asthma by reducing allergic airway inflammation and Th2-mediated immune responses, and the water-extracted polysaccharides of ginger could decrease coughing times, which were induced by citric acid.

In patients with acute respiratory distress syndrome (ARDS), an enteral diet with ginger contributed to gas exchange and reduced the duration of mechanical ventilation. This indicates the bioactive compounds of ginger have a protective effect against respiratory disorders, at least mediating them through the induction of relaxation in airway smooth muscles and the attenuation of airway resistance and inflammation.^[4]

Pipera longa (fam: Piperaceae) is an important plant in several indigenous systems of medicine. Especially in ayurvedic preparations, which are meant to have an effect on respiratory disorders, *Pipera longa* is commonly called long pepper, and it is locally known as Thippalli or Pippalli. The vast applications of long pepper made it an abundant ingredient in the various medicinal formulations of traditional medicines. The long pepper or thippalli has been used throughout history as a part of food, botanical portions, powders, etc., which has varying success in the treatment and prevention of several diseases. Thippalli is a powerful stimulant for both the respiratory and digestive systems. It also shows a reviving effect on the lungs. For the treatment of

various diseases and infections, fruit and root plants are used. It is widely used as an expectorant, a cold suppressant, a medullary stimulant, and also for conditions like asthma, nausea, and diarrhea. Various scientific studies proved that the fruit of *Piper longum* has properties like anti-inflammatory, anti-allergic, and hypoglycemic actions. Anti-fertility potential was only in the roots of the plant.

Piper longum has a variety of chemical constituents, of which piperine is the chief alkaloid present. The fruit of long pepper consists of a large number of phytoconstituents like alkaloids and amides, such as methyl piperine, isoperonaline, piperettine, asarinine, piperlongumine, piperlonguminine, etc. A complex mixture of caryophyllene, pentadecane, and bisabolone is the volatile oil present in the long pepper. Essential oils have insecticidal and insect repellent activities. Lignans and esters are also present in various proportions in the long pepper. The pharmacological activities of piperine include anti-inflammatory, anti-metastatic, anti-cancer, larvicidal, leishmanicidal, immunosuppressive, anti-mycobacterial, and antiparasitic. It is known to stimulate the digestive enzymes of the pancreas, protect against oxidative damage, lower lipid peroxidation, and mainly improve the bioavailability of many therapeutic drugs. Piperine was found to prevent the development of characteristics of asthma that included airway hyperresponsiveness, airway and airway eosinophilia, and lung inflammation in an ovalbumin-induced asthma model.^{[5][6]}

III. METHODOLOGY

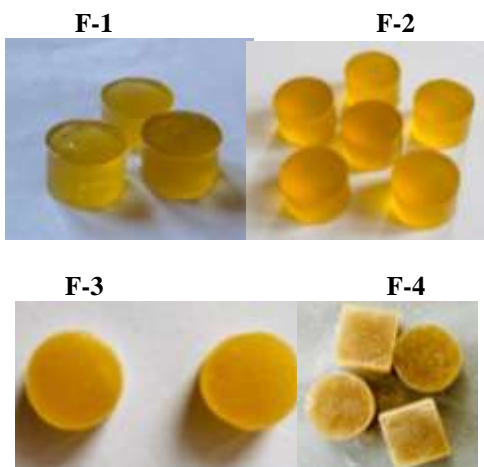
The first and initial step of the study was the identification of the *Justicia adhatoda* plant by a botanist. After that, we collected fresh leaves of *vasaka* and cleaned them properly using fresh water. Wipe out the excess water content from the leaves surface using a clean cotton cloth/tissue. 100 grams of leaves are ground into a rough paste using a mortar and pestle with 100 ml of distilled water. By using four layers of muslin cloth, the paste obtained by grinding is filtered. The filtrate obtained is the *vasaka* leaf extract, which is stored in an air tight container at 4°C for experimental use. The extract of dry ginger and long pepper was done by the Soxhlet extraction method. 50 grams of crushed dry ginger powder and long pepper were placed in a separate soxhlet apparatus in a packet. Hydro-Alcohol solvent system used for both extraction. 200 ml of ethanol and water (4:1) are used as solvent systems for the extraction of dry ginger and it is refluxed for 10 hours. 250 ml of the same solvent system for

long pepper extraction and it is reflexed for 12 hours. The obtained extract of dry ginger and long pepper is concentrated separately in a water bath

until a semi solid constancy is obtained and stored in the refrigerator in an air tight container for further studies.^{[7][8][9][10]}

Formulation of Nutraceutical Gummies

Ingredients	Formula 1(gm)	Formula 2(gm)	Formula 3(gm)	Formula 4(gm)
Vasaka leaves extract	0.8	0.6	1.2	1.2
Dry Ginger extract	0.5	0.2	0.5	0.5
Long pepper extract	0.2	0.2	0.2	0.2
Gelatin	20	20	20	15
Sugar Syrup	100	100	100	100
Honey	0.5	0.5	1	1
Flavoring Agent	10	25	100	100
Distilled Water	Qs.	Qs.	Qs.	Qs.
Sodium benzoate	0.1	0.01	-	-
Methyl Paraben	-	-	0.01	-
Corn Starch	-	-	Qs.	Qs.
Agar	-	-	-	5



By comparing the above 4 formulations, Formula 3 was found to be more stable and acceptable.

IV. PROCEDURE

Sugar syrup was prepared by 66gm of

sugar and 34 ml of distilled water. Orange juice was the flavouring agent used in the formulation to mask

the bitter and pungent taste of herbal extracts.

Preparation of nutraceutical gummy: Gelatin was bloomed using half portion orange juice. Add next half of the juice in to bloomed gelatin and dissolved using water bath and add methyl paraben. The temperature was maintained at 65°C. Add herbal extracts in the desired quantity into the sugar syrup and the sugar syrup mixture was transferred in to the gelatin solution. Transfer the gummy mixture into a sterile silicon mould. Refrigerate the mould for overnight at 10°C. Unmould the gummies and coat with corn starch. Store the starch coated gummies in an air tight sterile container and store at cool temperature.^{[11][12]}

V. EVALUATION STUDIES

- Physical appearance/visual inspection:** The formulation prepared was evaluated for clarity, texture, and consistency.
- Determination of pH:** A 10% v/v Gummy solution was constituted in distilled water, and the pH of the solution was measured using a calibrated pH meter.
- Solubility test:** Solubility was obtained by adding the solute in a small amount to a fixed volume of solvents like water, ethanol, ether, and 0.1 N HCl during the pre-formulation solubility analysis.
- Stability study:** The stability of the formulation was studied for a period of 4 weeks by keeping it at a temperature of 25–30 °C.

- Microbial examination:** The melted gummy base was struck into the sterile Petri dish under aseptic conditions. The plates were incubated at 37°C for 24 hours and observed for microbial
- Moisture content:** The moisture content was determined by drying finely grounded samples (10 g) in a hot air oven at 105 °C until a constant weight was achieved
- Stickiness:** The texture of the medicated jelly in terms of stickiness had been evaluated by visual inspection of the product after mildly rubbing the jelly sample between two fingers.
- Spreadability:** The spreadability of jelly was tested by placing it between two slides with a 1000 g weight and pressing it for 5 minutes to a consistent The spreading area of the jelly was then estimated using the equation ($A = \pi r^2$), which is represented as the area of a circle.
- Weight variation:** The jellies were removed from the moulds and weighed. The observed data was reported as mean standard deviation (SD), with the average weight of 10 jellies being used as the reference point.^{[11][12][13]}

VI. RESULTS AND DISCUSSION

1. Chemical Test:

Chemical test for Alkaloid (Vasicine and piperine) and Phenols (Gingerol) was performed and presence of alkaloids and phenols in the prepared gummy was confirmed.

Chemical test for Alkaloids:

Test	Inference	
	Vasicine	Piperine
Mayor's test	+ve	+ve
Hager's test	+ve	+ve
Dragendroff's test:	+ve	+ve
Wagner's test:	+ve	+ve

Chemical test for Phenols:

Test	Inference
Litmus test	+ve
Ferric chloride test	+ve
Bromine water test	+ve

2. Physical appearance:

Sl no.	Parameter	Result
1.	Colour	Yellowish Orange
2.	Odour	Fruity
3.	Texture	Soft
4.	Clarity	Opaque
5.	Consistency	Semisolid
6.	Taste	Sweet and spicy

3. Determination of pH: The taste and stability of oral jellies are influenced by the formulation's pH. The pH of the generated jellies was determined to be in the range of 4.3 to 4.1, which was slightly acidic.

4. Solubility test:

Solvent	Solubility Behaviour
Water	Sparingly soluble
Ethanol	Soluble
Ether	Slightly soluble
0.1 n hcl	Easily soluble

5. Moisture content:

Time	F1	F2	F3	F4
0 min	1.9 gm	2.02 gm	2.07 gm	2.1 gm
5 min	1.6 gm	2 gm	2.03 gm	2.02 gm
10 min	1.2 gm	1.9 gm	2 gm	2 gm
15 min	1.05 gm	1.7 gm	1.98 gm	1.8 gm
20 min	1.02 gm	1.5 gm	1.96 gm	1.7 gm
25 min	1 gm	1.4 gm	1.95 gm	1.5 gm
30 min	0.9 gm	1.3 gm	1.95 gm	1.5 gm
35 min	0.9 gm	1.3 gm	1.95 gm	1.5 gm

Moisture content = Initial weight – Final weight

- F1 ➔ $1.9 - 0.9 = 1$ gm
- F2 ➔ $2.02 - 1.3 = 0.72$ gm
- F3 ➔ $2.07 - 1.95 = 0.12$ gm
- F4 ➔ $2.1 - 1.5 = 0.6$ gm

6. Stickiness:

Formulation	Stickiness
F1	Gluey
F2	Sticky
F3	Non-sticky
F4	Non-sticky

7. Spreadability:

Formulation	Initial area	Spreadability(cm ²)
F1	1.13 cm ²	9.61 cm ²
F2		6.60 cm ²
F3		3.46 cm ²
F4		2.54 cm ²

8. Weight variation:

The average weight of the Gummy Formulations was found to be:

Formulation code	Average weight
F1	1.9
F2	2.02
F3	2.07
F4	2.1

9. Microbial Examination:

In the control medium growth of microorganism has observed and in the test medium minimal growth is produced. Which can be concluded by the proof of sterility of the formulation and antimicrobial activity of product.

10. Stability study:

The gummy preparation was found to be stable throughout the 4-week study at room temperature and at 4° C.

VII. CONCLUSION

Hereby mentioned data revealed that Formula 3 has shown the effective characteristic features of the oral gummies throughout the research period. The gummies had good homogeneity, pH, non-stickiness, consistency, spreadability and palatability. The activity of added herbal extracts was previously proven by others. The key extract was Vasaka extract, in which the main active constituent is vasicine. The presence of vasicine in the vasaka leaf extract was identified. And vasicine is a potent Broncho dilator. Hence it is useful for enhancing the pulmonary functions and relief from Broncho construction ailments.

The future benefit or advantage of herbal oral gummies is that the plants used in our formulation are easily available and are also already being used from ancient times and traditional medicines. The polyherbal oral gummy formulated using herbal extracts is safer than using synthetic one, since it increases patient compliance.

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