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Formulation and Evaluation of Ivy Leafs Dry Extract with Dexamethasone Antitussive Natural Cough Syrup

Nikita Mule, Komal Padme, Dr. Nandu Kayande
Thakur Shivkumar Singh Memorial Pharmacy Collage, Burhanpur, MP, India

Abstract: *Acute cough due to viral upper respiratory tract infections (URTIs) and bronchitis is a common reason for patients to seek medical care. Non-antibiotic over-the-counter cough medications such as ivy leaf extract are frequently used but their efficacy is uncertain. Our purpose was to update our previous systematic review and evaluate the effectiveness and tolerability of ivy leaf in the treatment of acute URTIs in adult and paediatric populations. The clinical effects of Hedera helix have been investigated in a total of more than 20 clinical studies mostly in children suffering from upper airway infections. Ivy leaves (Hedera Helix) dry extract with Dexamethasone antitussive natural cough syrup. The pharmacological result also demonstrates that ivy leaves (Hedera Helix) and dexamethasone cough syrup are more effective in relieving cough due to the presence of triterpene saponins. Ivy leaves dry extract with dexamethasone cough syrup for the treatment of different disease of the respiratory tract system and include catarrh of the respiratory passages; symptomatic treatment of chronic inflammatory bronchial illnesses ; and acute inflammation of the respiratory tract accompanied by coughing (HMPC Assessment).*

Keywords: URTIs, Hedera helix, HMPC, Antitussive.

I. INTRODUCTION

1.1 Liquid Dosage Forms

- Liquid dosage forms reach large scale production after being pre-formulated at the laboratory level followed by formulation at the small scale and then at the pilot plant scale. Due to the complexity of the manufacturing process, scale – upfrom pilot to commercial production is not a simple extrapolation. The approaches to the four levels of production are different. Most of the formulation ingredients are analysed, studied, and selected at the laboratory scale. While small - scale production is more focused on the liquid preparation procedure with higher amounts of ingredients, the main issues at the pilot plant scale are the design of infrastructure and reduction of costs. Commercial production introduces problems that are not a major issuon a small scale, for instance, materials handling and storage, pulverizing, mixing, dissipation of the generated heat during production, time control, personnel administration, and bottle - filling capabilities. Furthermore, purified water is essential for the manufacturing of these products as well as on- site packing capabilities.
- Oral Liquid Dosage Forms in Pharmaceuticals including Syrup, Oral Suspension, Oral Solution, Oral Drop, Oral Emulsion, Mixture, Linctuse and Elixir.
- Oral liquids are homogeneous liquid preparations, usually contains a solution, Oral Liquids should not be diluted and stored after dilution unless the individual monograph directs for dilution. Diluted oral liquids may not be stable for long period physically and chemically so it should be diluted freshly or should be used within the period as stated on the label. (**MARCH 05, 2019Mantanus J, Lebrun P)**
- Liquid state forms are meant for internal, parental or external use. They are available in monophasic and biphasic forms. Monophasic liquid dosage forms order soma pills are true or colloidal solution. Water is mainly used as a solvent for majority of monophasic liquid dosage forms. The liquid which consists of two phases order soma global delivery are known as biphasic liquids.

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Classification of liquid dosage form:- Basically, liquid dosage forms are divided into Two parts according to phase.

- Monophasic liquid dosage forms
- Biphasic liquid dosage forms

Uses of liquid dosage form

- Internal Use- Syrup, mixture, linctuses, elixirs, parenteral preparations.
- External use- Gargle, mouthwash, lotions, nasal drops, eardrops.

II. SYRUP

The syrup is a vicious oral liquid that contains one or more active ingredients in solution. The base generally contains large amounts of sucrose or other sugars to which sorbitol may be added to inhibit crystallization or to modify solubilisation, taste and other base properties. Sugarless syrups may contain other sweetening agents as saccharin and thickening agents. Syrups may contain ethanol (95%) as a preservative or as a solvent for Flavours. Antimicrobial agents may also be added to syrups to maintain the microbial quality of preparation.
(Ziemonas,E,MantanusJBiomedicalAnalysis2010.)

Advantages of Syrup

1. The active agent in homogeneously dispersed through the product.
2. The dose of the active agent in easily adjusted by measuring a different volume.
3. They are attractive in appearance and gives beneficial psychological effects.
4. The liquid dosage form is expected for certain types of product like cough medicaments.

Disadvantages of Syrup

1. As a consequence of this , the solution product has a shorter shelf life than the intended solid formulation.
2. Liquid dosage forms may requires special storage facilities in very cold or very hot condition.
3. Palatable sweet – a vehicle for bitter/Nauseous substance.

III. DRUG PROFILE

Dexamethasone –

Dexamethasone is a corticosteroid that prevents the release of substances in the body that cause inflammation. Dexamethasone is used to treat many different inflammatory conditions such as allergic disorder . It is used to treat condition such as arthritis blood/hormones disorders , immune system disorder.

Ivy Leaves Dry Extract

Ivy leaves dry extract is an expectorant containing dry ivy leafs extract . It works by thinning and loosening phlegm or mucus in the lungs, windpipe and nasal passage ,thereby helping to cough out easily. It soothes the airway as well. Ivy leafs extract contains saponins which are believed to have expectorant properties.
In vitro studies of ivy leaves show evidence of potential broncho dilating activity , anti inflammatory effect and antitussive properties.

Preformulation study of Drug (Dexamethasone)

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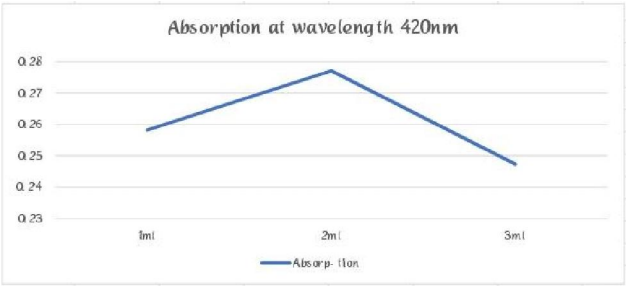
Identification Test of Drug

- Odour :- Odourless
- Colour :- off white crystalline
- Solubility:- soluble in water
- Stability : - Hygroscopic
- Taste : - Bitter

- **Melting point of dexamethasone** :-Melting point was found to be in range 261±1.235°C.
- **Boiling point of dexamethasone**:- Boiling point was found to be at 760mm Hg.
- **Analytical method of drug**:-Analytical methods are intended to establish the identity, purity, physical characteristics and potency of drugs. Methods are developed to support drug testing against specifications during manufacturing and quality release operations, as well as during long-term stability studies .
- **Absorption of Dexamethasone sodium phosphate by UV Spectrometer -** Standard Solution of Dexamethasone sodium phosphate: Standard Dexamethasone sodium phosphate of 10mg was accurately weighed and transferred to 10ml volumetric flask. It was dissolved properly and diluted to mark with distilled water to obtain concentration of 1mg/ml. This solution was used as stock solution. From this, working standard solution and suitable dilutions were prepared. Determination of Absorption Maxima: By the appropriate dilution of standard drug solution with distilled water, solution contain 10µg/ml of Dexamethasone sodium phosphate was scanned in the range of 200-400nm to determine the wavelength of maximum Absorption. Drug shows absorption maxima at 242 nm.
- **Calibration of drug** -Procedure: Aliquots of standard solution of Dexamethasone sodium phosphate ranging from 0.5-2.5 (1ml=100µg) were transferred in to a series of 10ml volumetric flasks. To each flask required amount of distilled water was added and finally the volume in each flask was brought up to the 10ml with the distilled water. Then Absorbance's were measured at 242nm against the reagent blank. Then Calibration curve data is indicate in table –

S.no.	Congratulations	Absorption
1.	1ml	0.258
2.	2ml	0.277
3.	3ml	0.247

Calibration data of Dexamethasone drug (calibration curve)



- **Partition coefficient of drug:** Dexamethasone weighed amount of drug (10mg) was taken in a Separating funnel containing 50 ml of n-Octanol and 50 ml of PBS (pH 7.4). The partition coefficient of dexamethasone was found to be 1.818±0.034 (Specification - 1.83). When the value of log p of a compound is greater than 1is Lipophilic but the value is less than 1 is Hydrophilic in nature. Partition Coefficient of Dexamethasone was found to be 1.818 so it is Lipophilic in nature.
- **Determination of pH (1% w/v solution in water):-** The pH of dexamethasone was found to be 6.1±0.234.
- **Drug-Excipients compatibility study** :-Incompatibility studies were done by a stress at different temperatures such as freezer (10°C-20°C), Cold (2°C-8°C) and room temperature, using refrigerator with 1:1 ratio of Drug

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and excipients. The study was carried out for one month observed for the physical changes such as colour, liquefaction etc.

- **Solubility determination**:-- Dexamethasone was freely soluble in Ethanol, Methanol, Acetone and Dimethyl Sulphoxide (DMSO) and slightly soluble in Water and PBs.

S.no.	Solvent	Solubility
1.	Ethanol	++++
2.	Water	+
3.	Methanol	++++
4.	Acetone	+++

- **Flow Properties:** Bulk Density and Tapped Density - Density compressible blend was pured gently through a glass funnel into a graduate cylinder of bulk density appratous , Then bulk density and Tapped Density were calculated .
  Bulk density = Weight of sample in gm/ Find volume of sample contained in cylinder

  Tapped Density = Weight of sample in gm /Tapped density final volume after tapping in cylinder

- **Carr's index** – Used to compare the bulk density and tapped density. The Compressibility index was calculated by the formula.
  Carr's index = (Tapped density – Bulk Density) / Tapped density × 100

- **Housner Ratio:** The flow preparation of bland , granules or powder are measured by this Ratio .
  Housner Ratio= Tapped Density / Bulk Density

- **Angle of Repose**: Angle of Repose with care, Dynamic angle of response measurements can be replicated with relative standard deviations of approximately 2% they are particularly sensitive to change in partical sieve distribution and the moisture content and they provide rapid means of monitoring significant batch difference in these respective.
  (Aarti Hardia, Amisha Mahajan2, Aashish Hardia Volume 10, Issue 3, 1818 1827.ISSN2277.)

IV. MATERIAL

1. I brought all the required Chemicals and drug materials from Narmada Scientific Corporation Pvt Ltd S.K. Tranders Pvt Ltd. P.K. Scientific Indore Pvt Ltd At Thakur Shivkumar Singh Memorial Pharmacy Collage Ziri Burhanpur (M.P.)
2. The powder of Ivy Leaves (Hedera helix) dry extract was purchased online from Flipkart.in

4.1 Method

Pharmaceutical syrup are produced by mixing purified water , sweeteners ,active ingredients (API), aromas , Flavours and otheringredients e.t.c.

Procedure

Preparation of cough syrup Methylparaben and propylparaben were added to the rose water and mixed until a clear solution was formed.In aseparate glass, the xanthan gum was soaked in a small amount of rose water. Sorbitol, glycerin and propylene glycol were mixed, then sucralose and honey flavor were added, after the completion of mixing, ivy leaf extract was added. Finally, mixed all of the above solutions in a separate beaker. Then added the potassium sorbate and citric acid. Then added active drug Dexamethasone and Heat until a clear solution is obtained. Add a volume of rose water to make 1l syrup.

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Table 1: COMPOSITIONOF ANTITUSSIVE COUGH SYRUP A1,A2,A3 and A4 :-

S. No.	Ingredient	Used as	Amount (Gram)
1.	Methylparaben	Preservative	1.20
2.	Propylparaben	Preservative	0.20
3.	Potassium sorbate	Pharmaceutical preservative	1.50
4.	Xanthan gum	Thickening agent	2.50
5.	Citric acid	Preservative	0.70
6.	Ivy leaf extract	Active ingredients	7.14
7.	Sorbitol	Sweetener (Diet sugar)	200.0
8.	Glycerine	Soothing agent	25.0
9.	Propylene glycol	Non-active enabling agent or excipient	50.0
10.	Sucralose	Artificial sweetener	1.50
11.	Propylene glycol	Non-active enabling agent or excipient	50.0
12.	Dexamethasone	Active ingredients	0.10
13.	• Rosewater (lab distilled) for A1 • 50%lab distilled rose water + 50% distilled water) for A2 • Rosewater (marketed) for A3 • 50% marketed rose water + 50% distilled water for A4	Active ingredients	Q.S for 1 l

https://www.researchgate.net/publication/354362193_Formulation_and_evaluation_of_natural_antitussive_cough_syrups

Evaluation Parameters

a. PH Measurements: The pH of syrup is measured using by the pH paper which range was found to be a 6-7 .

b. Viscosity: U-tube viscometers are also known as glass capillary viscometers or Ostwald viscometers. A viscometer consists of two reservoir bulbs and a capillary tube. In one arm of the U is the capillary, a vertical section of a precise narrow bore. Above, which is a bulb, and with it is another bulb lower down on the other arm, as shown in the image.

C. Physical Stability: The syrup must be clear no solid particles was present in syrup.

d. Solubility: The Solubility of syrup was determined and it was Soluble in water.

e. Dissolution Rate: The dissolution Rate of syrup was determined and it was dissolved in HCl.

f. Refractive index: The Refractive index of the syrup was determined and It range was found to be 1.4608-1.4630

g. Determination of Sucrose Concentration:- Concentration of sucrose is very important in syrup because high amount of sucrose in syrup may cause crystalline of syrup while low amount may cause loss of preservatives proper of syrup. Theconcentration of sucrose in determineusing analytical tools UV Spectrophotometer.

h. Light Transmittance Test :- A light Transmittance meter is used to check the color of syrup. In this Syrup sample is checked for color by passing the light is compared to light Transmittance rates for different grades.

I. Organoleptic Test:

- Taste examination- A pinch of final syrup was taken and examined for its taste on taste buds of the tongue.
- Odour examination -Odour examination Two ml of final syrup was smelled individually. The time interval among two smelling was kept 2 minutes to nullify the effect of previous smelling.
- Color examination - Color examination Five ml final syrup was taken into watch glasses and placed against white back ground inwhite tube light. It was observed for itscolor by naked eye.

https://remixeducation.in/evaluation-of-syrup.

V. RESULT AND DISCUSSION

- **Drug and excipients compatibility**: The DSC Thermo gram ,ml of the pure drug, chemical and excipients . HPMC mixture and good compatibility with excipients.
- **Drug Content**: 1 ml of the prepared syrup was measure accurately and dissolved in 10 ml of water and was then filtered was taken and was diluted up to 100ml by PH 7.2 and was observed in the UV SPECTROMETER at 257 nm.

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5.1 Discussion

The antitussives activity of cough syrup formulation A1,A2, A3 and A4 at 3 different dose 5ml/70kg , 10ml/70kg. , And 15ml/70kg , control and standard were mentioned in graph of antitussive cough syrup from A1,A2,A3 and A4 standard drug on sulphur dioxide S02 induced cough.

TABLE 2: Antitussive Activity Of Cough Syrup Formulationa1, A2, A3 and A4 And Standard Drug On So2 Induced Cough.

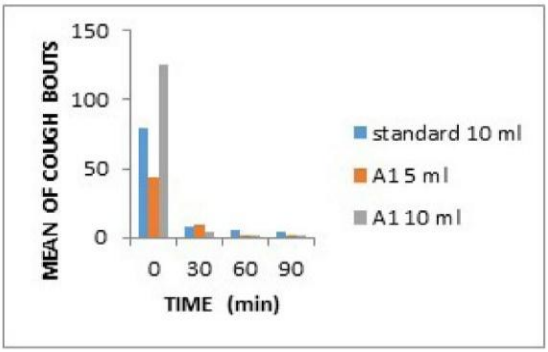

Fig. 1 : A1 formulation SO_2 induced cough method

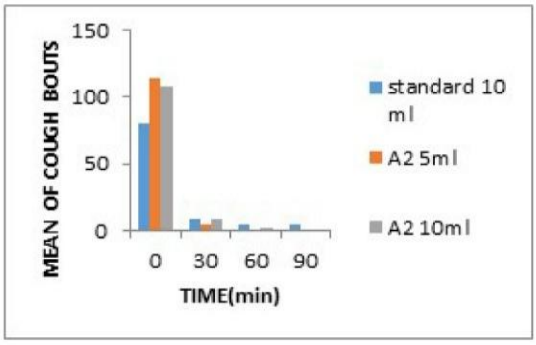

Fig. 2 : A2 formulation SO_2 induced cough method

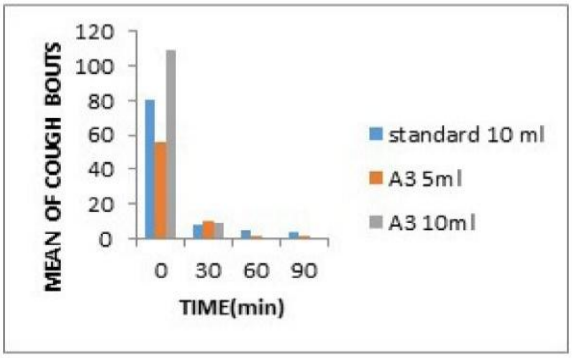

Fig. 3 : A3 formulation SO_2 induced cough method

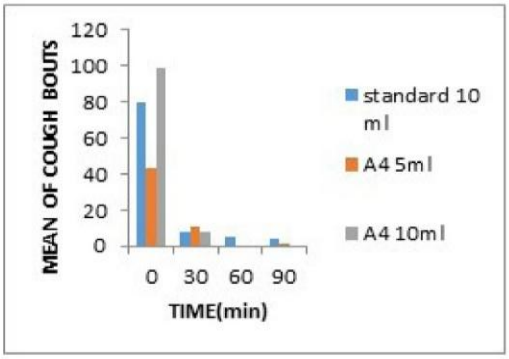

Fig. 4 : A4 formulation SO_2 induced cough method

- **Statical Analysis:** The result communicated as standard deviations SPSS Adaption 20.0 single direction investigation of change (ANOVA) post .The result show after 60&90 min. All model showed significant suppression of cough $P<0.05$.

5.2 Result

The antitussive activity of cough syrup formulation A1, A2, A3 and A4 at 3 different doses 5ml/70kg, 10ml/70kg and 15ml/70kg control and standard were mentioned in graph of antitussive cough for A1,A2,A3 and A4 and standard drug on sulphur dioxide (SO2) Induced cough.

VI. CONCLUSION

Ivy leaves dry extract and Dexamethasone is traditionally used to manage the cough .In the present study ivy leaves achieved therapeutic effect to relieve cough and Reduce airway inflammation. The pharmacological result also demonstrates that ivy leaves (Hedera Helix) and dexamethasone was more effective in relieving cough due to the presence of triterpene saponins.

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