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FORMULATION OF MULTICOMPONENT COLD AND COUGH SYRUP

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ABSTRACT

The Multicomponent syrup formulation of the present experiment contains one or more other drugs for obtaining more than one therapeutic result from a single dose. An antitussive drug such as codeine, pholcodeine. Noscapine, Dextromethorphan, Chlophedianol are used for relief in coughing. These are mostly opoids and non opoids. Non-narcotic antitussives include which is a synthetic derivative of morphine with no analgesic or sedative properties and which is usually included as a constituent of many compound cough preparations sold over the counter. It is a synthetic derivative of morphine with no analgesic or sedative properties. It is as effective as codeine in suppressing acute and chronic cough when given orally. Further, nasal decongestant is incorporated for relief of the upper airway congestion often accompanying disorders such as rhinitis and upper respiratory infections. Many H1 antihistamines have been conventionally incorporated to antitussive/ expectorant formulations. They effort relief in cough due to their sedative and anticholinergic actions, but lack selectivity for cough centre. They have no expectorant action, may even reduce secretions by anticholinergic actions. Example, Chlorpheniramine, Diphenhydramine, promethazine etc. Therefore, formulation containing antitussive, nasal decongestant and antihistamine can avoid need of drug taking separately. This will lead to reduce frequency of administration and increased patient compliance.

KEYWORDS: Multicomponent syrup, Chlorpheniramine, Diphenhydramine, anticholinergic actions.

INTRODUCTION

A cough in children may be either a normal physiological reflex or due to an underlying cause. In healthy children it may be normal in the absence of any disease to cough ten times a day. The most common cause of an acute or sub acute cough is a viral respiratory tract infection. In adults with a chronic cough, i.e. a cough longer than eight week, more than 90% of cases are due to post-nasal drip, asthma, eosinophilic bronchitis, and gastro esophageal reflux disease. The cause of chronic cough is similar in children with the addition of bacterial bronchitis. A syrup is a thick, viscous liquid consisting primarily of a solution of a sugar in water, containing a large amount of dissolve sugars but showing little tendency to deposit crystals. The viscosity arises from the multiple hydrogen bonds between the dissolved sugars, which has many hydroxyl (OH) groups and the water.

ADVANTAGES

- children and some adults have difficulty in swallowing tablets and capsules.
- Young They are more quickly effective than, for example, tablets, which must disintegrate in the body before absorption can begin.
- Absorption is not delayed while solution takes place in the gut.(contrast solid dosage forms and oral suspensions).
- Uniform dosage is certain (contrast suspensions and emulsions where uneven dosage is possible if the patient fails to shake the bottle).
- They provide a safe means of administering substances like potassium iodide.
  - and bromide that cause gastric pain if taken dry, e.g. as powders or tablets.
- The attractive appearance of a solution in a well polished bottle has a beneficial.
- Psychological effect.

DISADVANTAGES

- They are less stable than solid dosage forms since deleterious changes take.
  - Place more readily in solution.
- Unpleasant flavors can be difficult to mask.
- They are bulky to carry around.
- A spoon is needed to administer the dose.

Pharmaceutical solutions for oral administration are unsuitable for therapeutic agents that are chemically unstable in the presence of water.

MEDICATIONS FOR COLD AND COUGH

I. Pharyngeal demulcent: Lozenges, cough drops, linctuses containing Syrup, glycerine, liquorice.

II. Expectorants (mucolytics)

a. Bronchial secretion enhancer:

Sodium or potassium citrate, potassium iodide, guaifenesin, balsam of tolu, Vasaka, ammonium chloride

b. Mucolytics: Bromhexine, ambroxol, Acetyl cysteine, carbocysteine.

III. Antitussives (cough centre suppressants)

a. Opioids: codeine, pholcodeine**.**

b. Non Opioids**:** Noscapine, dextromethorphan, Chlophedianol.

c. Antihistamines: Chlorpheniramine, Diphenhydramine, Promethazine.

d. Adjuvant Antitussives: Bronchodialators e.g. Salbutamol, terbutaline.

CLASSIFICATION OF SYRUP

a) Simple syrup

b) Sorbitol syrup

c) Medicated syrup

d) Artificial syrup

e) Dextrose base syrup

f) Invert syrup

Advantages of Multicomponent product

I. Multicomponent product is a more convenient.

II. It is less expensive.

III. Patient complience.

IV. Avoid abused of single ingredient control drug substances.

V. Multicomponent reduced pack size, dose of drug with achieve same efficacy as like combination all single ingredient product.

VI. Reduce frequency of drug.

Need of Multicomponent System

1. There are many cough and cold remedies available on the pharmacy since no single ingredient medication can address all the symptoms experienced by the patient ,combination

products are very popular, when a combination product is used it is important to select a product most suited to the individual patient, as not all patients need every ingredient.

2. Treatment of cough and cold generally needs a symptomatic treatment. Several symptom of cough, nasal decongestant, histamine release, allergic rhinitis, rhinorrhoea treating each symptom separately by taking drug for each condition is difficult. Instead of that take one medicine that relives all symptoms.

3. Our combination used antitussive, nasal decongestant, antihistamine. It treat cough and cold blocked and runny nose, sneezing, watery eyes, cough, nasal congestion, pain or headache, i.e. patient no need to take single drug.

FORMULATION CONSTITUENTS

Pharmaceutical solutions may contain a range of excipients, each with a defined Pharmaceutical purpose. Examples of these include:

I. Vehicle

Vehicles, in pharmaceutical formulations, are the liquid bases that carry drugs and other excipients in dissolved or dispersed state. Pharmaceutical vehicles can be classified as under; Aqueous vehicles: Water, hydro-alcoholic, polyhydric alcohols and buffers. These may be thin liquids, thick syrupy liquids, mucilage or hydrocolloidal bases. Oily vehicles: Vegetable oils, mineral oils, organic oily bases or emulsified bases.

Eg. Water, polyhydric alcohol, buffers, etc.

a. Aqueous vehicle

Purified water USP is allowed for usage as vehicle or as a component of vehicle for aqueous liquid formulations except for those intended for parenteral administration (injections). It is obtained by distillation, ion exchange treatment, reverse osmosis or any other suitable process from water complying with the Federal Environmental Protection Agency with respect to drinking water.

1. Glycerin

Glycerol (or Glycerin) is a clear, colorless liquid, with thick, syrupy consistence, oily to the touch, odorless, very sweet and slightly warm to the taste. When exposed to the air, it slowly abstracts moisture. Glycerin is used as vehicle in various pharmaceutical products like Elixir of Phosphoric acid, Solution of Ferric Ammonium Acetate, Mucilage of Tragacanth, Glycerin

of boric acid, Glycerin of tannic acid, and in many Extracts, Fluid Extracts, Syrups and Tinctures.

2. Propylene Glycol

Pharmaceutical grade of Propylene Glycol is monopropylene glycol (PG or MPG) with a specified purity greater than 99.8%. PG is an important ingredient for a multitude of uses, including:

I.	Oral solution	10-25%
II.	Parenterals	10-60%
III.	Topical preparation	5-8%
IV.	Humectants	15%
V.	Preservative	15-30%

II. Lipid-Based Delivery Vehicles

Lipid based delivery – vehicles are suited for liquid formulation of low water soluble drugs coming under class II or IV drugs. Benefits of these types of formulations are that lipids that keep a hydrophobic drug in solution may facilitate the dissolution and Absorption of the drug as the lipid vehicle is metabolized in the GI tract.

b. Solubilizers

Wetting Agents and Surfactants

These are used in liquid dosage forms to create a homogenous dispersion of solid particles in a liquid vehicle. Wetting agents are Surfactants (HLB Value 7 to 9) that when dissolved in water, lower the contact angle and aid in spread ability of water on the particles surface to displace the air layer at the surface and help in wetting and solubilisation.

Eg. Sodium lauryl sulphate, sorbitan monooleate, sorbitan monopalmitate.

1. pH Modifiers and Buffering Agents

The pH of an oral liquid formulation is a key point in many regards. Control of the formulation pH, could prevent large changes during storage. Therefore, most formulations utilize a buffer to control potential changes in the solution pH. A combination of buffers can also be used to gain a wider range of pH compared to the individual buffer alone. However, not all buffers are suitable for use in oral liquids. For example, a boric acid buffer may be used for optical and IV delivery but not in oral liquids because of its toxicity. Stability of formulation containing non-ionizable API may also depend on pH.

Eg. Buffers such as citrate, tartarate, and various phosphate salts.

2. Suspending Agents and Viscosity-modifying Agents

One of the most crucial factors involved in formulating a pharmaceutical suspension is the selection of an appropriate suspending agent. Suspending agents impart viscosity, and thus retard particle sedimentation. Other factors considered in the selection of the appropriate agent include desired rheological property, suspending ability in the system, chemical compatibility with other excipients, pH stability, length of time to hydrate, batch-to-batch reproducibility, and cost.

Eg. Hydroxy propyl methyl cellulose, sodium alginate, tragacanth, xantham gum, etc.

3. Preservatives

Microbiological contamination presents a significant health hazard in oral liquids. Therefore, the use of preservatives become inevitable to prevent the growth of microorganisms during the product's manufacture and shelf life, although it may be most desirable to develop a "preservative-free" formulation to address the increasing concerns about the biological activity of these compounds. Most formulations require some kind of preservative to ensure no microbial growth.

Eg. Methyl paraben, propyl paraben, benzyl alcohol, etc.

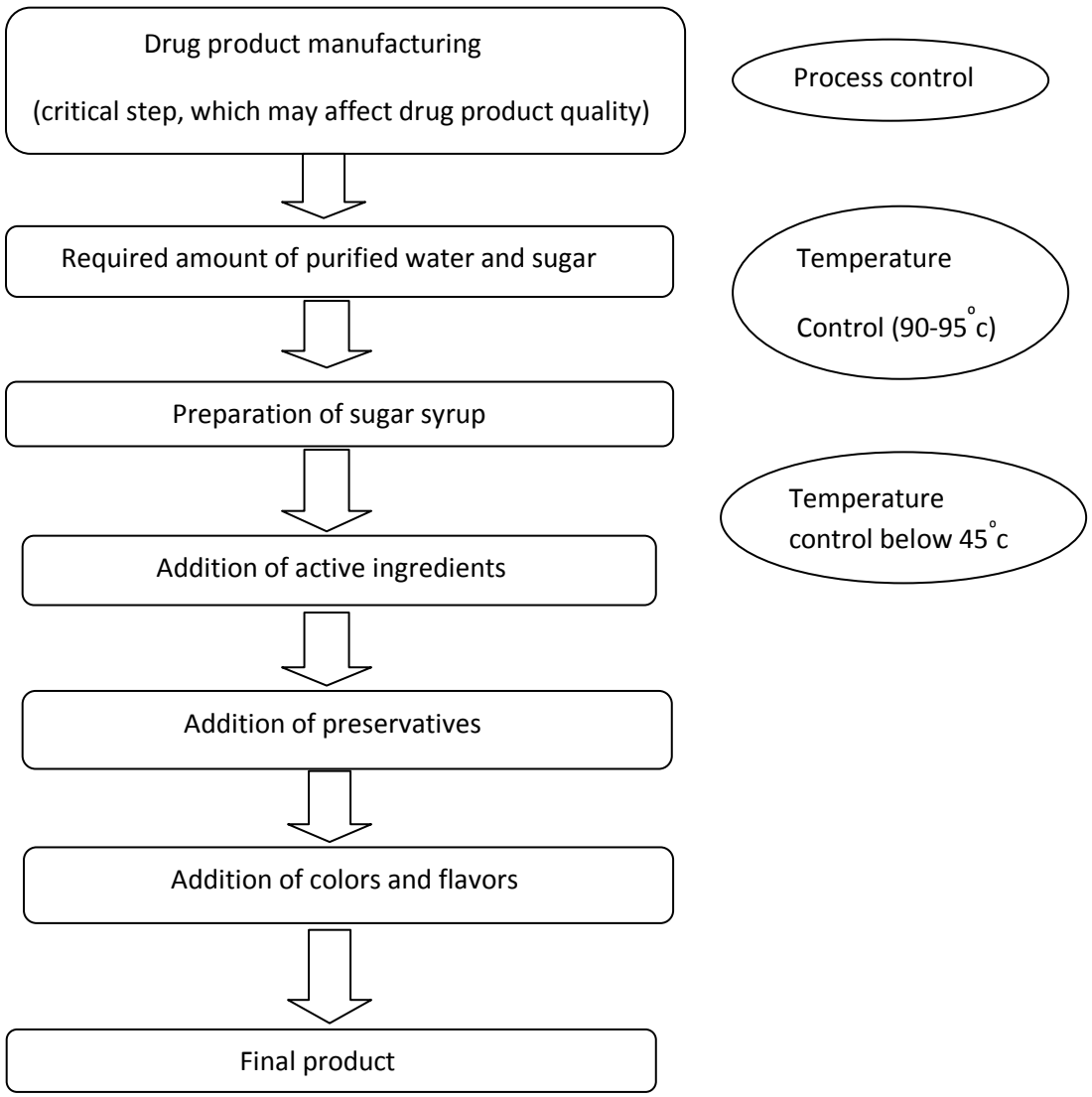
4. Stabilizers

Antioxidants

The oxidation of an API in an oral liquid formulation is difficult to control due to lowactivation energies (2-12kcal/mol) for oxidation and photolysis compared to solvolysis, dehydration, and polymorphic transformations (10-56kcal/mol). Antioxidants can be compounds that can reduce a drug that has been oxidized, or compounds that are more readily oxidized than the agents they are to protect (oxygen scavengers). Many of the lipid soluble antioxidants act as scavengers. Antioxidants can also act as chain terminators, reacting with free radicals in solution to stop the free-radical propagation cycle. Mixtures of chelating agents and antioxidants are often used because there appears to be a synergistic effect.

Eg. Ascorbic acid, sodium bisulfate, butylated Hydroxy tolune,etc.

Manufacturing process



EVALUATION TESTS TO BE PERFORMED IN MULTICOMPONENT SYRUP

1. pH bracketing study

➢ to study the effect of different pH on formulation.

2. Preservative bracketing study

➢ To study the effect of different concentration of preservative on formulation.

3. Microbial limit test

➢ To study the microbial attributes of finish product as per IP.

4. Force degradation study

➢ To study the degradation pathway and developing and validating suitable analytical methods by using forcing temperature-i.e 60^0c.

5. Photo stability study

   UV light :200 nm, fluorescence light 1.2 million Lux Hr.

- Evaluate the overall photosensitivity of the material for developing and validating suitable analytical methods and degradation pathway and ensures light does not result in unacceptable change.

6. Freeze thaw study (-20^0c)

- To study the effect of temperature change on finish product.

7. Rheology study

   Temp: 15^0c, 25^0c, 30^0c

- To study viscosity of finished product.

8. Sensory evaluation

- Flavor evaluation
- Taste evaluation

- To study and evaluation taste, mouth feels of finished products.

9. Combination of API

- To formulate physicochemically stable, clear formulation of syrup.

CONCLUSION

The overall objective of this project was to develop a multicomponent Cough and cold syrup. Syrups retard oxidation because it is partly hydrolyzed into reducing sugars such as sucrose, laevulose, dextrose and easier to swallow for children, old age and unconscious people. Cough is one of the most common symptoms encountered in clinical practice. There are many over-the-counter combination syrups available for the management of cough. These are the mainstay of therapy in case of nonspecific cough and may act as adjuvant in addition to treatment of the specific cause, in case of cough associated with other conditions. Combination of drugs in a formulation i.e. multicomponent form increases patient compliance and provides better therapeutic action as compared to the other single component system. This syrup is sugar based syrup which is prepared by solution with heat method. This is the usual method of making syrups when the valuable constituent is neither volatile nor injured by heat, and when it is desirable to make the syrup rapidly. The sucrose usually is added to the purified water or aqueous solution and heated until solution is affected, then it is strained and sufficient purified water is added to make the desired weight or volume.

Excessive heating of syrups at the boiling temperature is undesirable because more or less inversion of the sucrose occurs with an increased tendency to ferment (caramel). Different evaluation test are performed for the quality of the formulated syrup.

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