Formulation and Evaluation of Herbal Candy Based on Indian Medicinal Plants for Cancer Therapy via Immunomodulation

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ABSTRACT
Cancer is a hyperproliferative disorder which includes transformation, dysregulation of apoptosis, proliferation, invasion, angiogenesis and metastasis. Immunotherapy has provided new hope for cancer patients. Shankhpushpi, Brahmi, Nagarmotha, Chirata, Spirulina are used in Indian system of medicine for treating various health problems. All these medicinal plants used in the formulation have reported activity against different types of cancers. The present study deals with preparation of herbal candy as immune booster for cancer therapy by standard method. Candy is a fast and effective delivery system for medications. Hard boiled sugar candy was developed by using powder of crude drug. The phytochemical analysis of prepared herbal candy showed the presence of Carbohydrates, Alkaloids, Flavonoids, Terpenoids and Polyphenol. The results of physio-chemical and sensory characteristics of herbal candy revealed that candy prepared using sugar shows best consistency, mouldability, thread forming ability, brittleness along with desirable taste and colour at the temperature 145°C.

Keywords: Cancer, Spirulina, candy, Chirata, Brahmi.

INTRODUCTION
Cancer is the major public health problems and one of the leading causes of death in the world (1). Globally, the number of cancer deaths is projected to increase from 7.1 million in
2002 to 11.5 million in 2030\(^2\). There are several chemotherapeutic cytotoxic and immunomodulating agents are available to treat different types of cancer but these drugs are expensive, associated with serious side effects and morbidity. Still the research is continuing for an ideal treatment that has fewer side effects and is cost-effective. Herbs play an important role in treating different types of disorders\(^3\). Today only a limited number of plant products are being used to treat cancer. Indian medicinal plants and their constituent mediate their effect by modulating identified therapeutic targets. However medicinal plants require rediscovery in light of current knowledge of modern medicine. Shankhpushpi, Brahmi, Nagarmotha, Chirata, Spirulina are used in Indian system of medicine in various health problems and individually shows anticancer property.

The term ‘tonic’ is derived from the Greek word for tension: (tones). The designation ‘rob rant’ is often used synonymously and is derived from Latin ‘Rob rare’, which means ‘strengthen’\(^4\). The definition of tonic and its desired effects found in medical dictionaries and other resources very remarkably\(^5\). The tonic affects different organ systems and have different points of action\(^6\). Tonic perform various functions such as it fights infection, Strengthens tissue against micro-organism. Tonic Increases T-cell production and protects T-helper cells. It Stimulates macrophage capability.\(^7,8,9\).

The use of tonics may prove to be of high value in their prevention. These herbs contain bitter principles and mainly increase the secretion of digestive juices, especially in the stomach via primary stimulation of the bitter receptors in the taste buds at the base of the tongue and secondary gastrin secretion, which occurs when the bitter principles reach the stomach along with the food. Immunotherapy can be used alone or combined with other cancer treatment. Immunotherapy is treatment that uses a person's own immune system to fight cancer\(^11\). Immunotherapy improves immune system and destroy cancer cells\(^12\).

**ROLE OF SELECTED DRUG IN THE HERBAL CANDIES-**

The plants will be selected on the basis of their medicinal applications. Selected plants are discussed here\(^10\).

- **Convolvulus pluricaulis**- It consist of whole herb of *Convolvulus pluricaulis* belonging to family Convolvulaceae. Shankhpushpi having anti-stress, anti-anaxity, anti-depressive; properties are extremely useful for treating various disorders likes depression, restlessness and dementia. It increases function of brain\(^16,17\).
- **Centella asiatica (L.)** - It is the whole herb of *Centella asiatica* belonging to family Apiaceae. Bacoside B is a protein valued for nourishing the brain cells as a result Brahmi improves mental clarity, confidence, intelligence and memory recall. (17,18). Its main constituent asiaticoside possesses immunomodulatory activity, acting by increasing phagocytic index and total WBC count. In human peripheral blood mononuclear cells (PBMCs), Centella asiatica significantly increases proliferation and the production of IL-2 and TNF-α (30).

- **Cyperus rotundus** - It consist of dried rhizomes of *Cyperus rotundus* belonging to family Cyperaceae. It is used in treatment of fevers and digestive system disorders (19). It is also used in nausea, inflammation, for pain reduction, for muscle relaxation and for many
other disorders (21). It is also used as stimulant stomachic and tonic. In India it is used extensively as a raw ingredient in perfumery, aromatherapy and soap making (20).

- **Swerlia Chirata** - It is dried plant of *Swertia Chirata* belonging to family Gentianaceae. The drug having antispasmodic, antioxidant, anti-diabetic, antipyretic as well as antitussive activities. Moreover the different medicinal compounds were isolated from natural herbs effecting as anticancer, antitumor and anti-AIDS (22).

- **Spirulina** - Spirulina is a blue green algae Spirulina is rich in Vit. B contents and also possess beta carotenes. Spirulina has been reported to have immunostimulant activity, used in treatment of HIV, viral infection such herpes, cytomegalovirus, influenza, mumps and Measles virus. It lowers cholesterol and used in control blood pressure. (23). It is also used in weight loss. Spirulina is used against oral cancer (24).
MATERIALS AND METHODS

Selection of Herbs

Table-1: Herbs selected for the preparation of herbal candy are mentioned in the.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Biological name</th>
<th>Family</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shankhpushpi</td>
<td><em>Convolvulus pluricaulis</em></td>
<td>Convolvulaceae</td>
</tr>
<tr>
<td>Brahmi</td>
<td><em>Centella asiatica</em></td>
<td>Umbelliferae</td>
</tr>
<tr>
<td>Nagarmotha</td>
<td><em>Cyperus rotundus</em></td>
<td>Cyperaceae</td>
</tr>
<tr>
<td>Chirata</td>
<td><em>Swertia chirayita</em></td>
<td>Gentianaceae</td>
</tr>
<tr>
<td>Spirulina</td>
<td><em>Spirulina platensis or S. maxima</em></td>
<td>Oscillatoriaceae</td>
</tr>
</tbody>
</table>

Materials-

Table-2: Materials used for making candies

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ingredients</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shankhpushpi</td>
<td>70mg</td>
</tr>
<tr>
<td>2</td>
<td>Brahmi</td>
<td>70mg</td>
</tr>
<tr>
<td>3</td>
<td>Nagarmotha</td>
<td>30mg</td>
</tr>
<tr>
<td>4</td>
<td>Chirata</td>
<td>5.5mg</td>
</tr>
<tr>
<td>5</td>
<td>Spirulina</td>
<td>24.5mg</td>
</tr>
</tbody>
</table>
PROCEDURE FOR MAKING CANDY-

- Water and sugar were mixed in a deep bottom saucepan and allowed to boil, added slight butter and salt. Stirred the mixture with a wooden spoon.
- All powders were added one by one with the help of spatula with constant stirring.
- Flavoring agent and preservative were added to the mixture.
- Content was Poured immediately into the candy mold (Sprayed with vegetable oil so that the mixture does not stick with the wall of candy mold) and allowed to cooled by placing in the cooling racks.
- After cooling stored properly at a suitable temperature\(^{10,13,25}\)

<p>| | | |</p>
<table>
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<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>6</td>
<td>Sugar</td>
<td>85gm</td>
</tr>
<tr>
<td>7</td>
<td>Water</td>
<td>43ml</td>
</tr>
</tbody>
</table>

EVALUATIONS OF HERBAL CANDY

Quality Evaluation of Herbal Candy:

Sensory Evaluation of Herbal Candy:

The parameters for evaluation include appearance, colour, taste, flavour, consistency of herbal candy.
ANALYSIS OF HERBAL CANDY

Preliminary Phytochemical Analysis

Preliminary phytochemical analysis includes the tests for the presence of carbohydrates, proteins, glycosides, tannins, polyphenols and flavonoids in the prepared herbal candy by following standard procedures. The tests followed are as follows\(^{14,15}\).

Tests for carbohydrates

1. Tests for Carbohydrates
   a) Molish's test (General test):
   To crushed candy sample, added few drops of \(\alpha\)-naphthol solution in alcohol, shaken and added concentrated \(\text{H}_2\text{SO}_4\) from sides of the test tube was observed for violet ring at the junction of two liquids.

   b) Fehling's test:
   Crushed candy was treated with 1 ml Fehling's A and 1ml Fehling's B solutions mixed and boiled for one minute. Heated in boiling water bath for 5-10 min was observed for yellow, then brick red precipitate.

2. Tests for Steroids
   a) Salkowski reaction:
   1 gm of crushed candy was added to 2 ml chloroform and 2 ml concentrated \(\text{H}_2\text{SO}_4\) was added. Shake well, whether chloroform layer appeared red and acid layer showed greenish yellow fluorescence was observed.

   b) Libermann - Burchard test:
   1 gm of crushed candy was added to 1-2 ml acetic anhydride and 2 drops concentration \(\text{H}_2\text{SO}_4\) from the side of test tube observed for first red, then blue and finally green colour.

3. Tests for Alkaloids
   a) Dragendorff’s test:
   The crushed candy was treated with few drops Dragendorff’s reagent observed for orange brown precipitate.

   b) Mayer's test:
   The crushed candy was treated with few drops Mayer's reagent observed for precipitate.
c) **Hager's test:**
The crushed candy was treated with Hager’s reagent observed for yellow precipitate.

d) **Wagner's test:**
The crushed candy was treated with few drops of Wagner's reagent observed reddish brown precipitate.

4. **Tests for Flavonoids**
   a) **Shinoda test:**
   To powder candy, added 5 ml 95% ethanol, few drops concentrated HCl and 0.5 g magnesium turnings. Pink colour was observed.
   To small quantity of residue, added lead acetate solution observed for Yellow coloured precipitate. Addition of increasing amount of sodium hydroxide to the residue whether showed yellow colouration, which was decolourised after addition of acid was observed.

   b) **Ferric chloride test:**
   To powder candy, added few drops of ferric chloride solution observed for intense green colour.

5. **Tests for polyphenols**
   a) **Ferric chloride test:**
   1 gm of crushed candy was treated with 5% freshly prepared ferric chloride solution; deep blue colour came out \(^{(26)}\).
RESULTS AND DISCUSSION:
Cancer is treated by surgery, radiation therapy, chemotherapy, targeted therapy, Hormone therapy, Stem cell transplant, precision medicine and Immunotherapy to treat cancer\(^{(27)}\). Immunotherapy is a type of cancer treatment that helps your immune system fight cancer. The basic function of the immune system is to protect the individual against infectious agents and potential pathogens which puts the immune system in vital position between a healthy and diseased state of a host. Sensory evaluation revealed that polyherbal candies were brown in colour, sweet in taste, pleasant in odour with solid consistency. Phytochemical investigation of polyherbal candy showed the presence of Carbohydrates, alkaloids, flavonoids, terpenoids and polyphenols. The study was conducted to annotate the immunomodulatory potential of Indian medicinal plants. Results from this study showed that the polyherbal candy contain potential compounds that can initiate the production of antibodies in an immunosuppressed animal. Literature review explain the common usage of each individual herb as an immune stimulant and anticancer in the traditional medicine. Candy is a fast and effective delivery system for medications. Hard boiled sugar candy was developed by using powder of Shankhpushpi, Brahmi, Nagarmotha, Chirata and Spirulina. The results of physiochemical and sensory characteristics of herbal candy revealed that candy prepared using sugar. The temperature at 145ºC produced best consistency, mouldability, thread forming ability, brittleness along with desirable taste and colour. Further studies may be required to for rendering the combine immunostimulatory impacts. Herbal tonic candy formulation was subjected to various analytical techniques\(^{(15)}\).

- Sensory evaluation parameters revealed that brown in colour, with a sweet in taste.

**Table-3: Evaluation Test of candy**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>Brown</td>
</tr>
<tr>
<td>Test</td>
<td>Sweet</td>
</tr>
<tr>
<td>Flavour</td>
<td>Pleasant</td>
</tr>
<tr>
<td>Shape</td>
<td>Rose</td>
</tr>
<tr>
<td>Consistency</td>
<td>Solid</td>
</tr>
</tbody>
</table>
Phytochemical tests of herbal candy were determined and results were tabulated.

**Table-4: Phytochemical Test**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>Present</td>
</tr>
<tr>
<td>Alkaloids</td>
<td>Present</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>Present</td>
</tr>
<tr>
<td>Terpenoids</td>
<td>Present</td>
</tr>
<tr>
<td>Polyphenol</td>
<td>Present</td>
</tr>
</tbody>
</table>

**CONCLUSION**

The use of various plant specific dose during the scheduled regimen may be helpful in obtaining higher protective antibody against different infections including production and development of more effective cell mediate immune response for protection against various types of cancer. Herbal formulation may be therefore recommended for use as positive immunomodulator. Literature reveals that many of the Phyto-chemicals in the form of alkaloids, flavonoids, terpenoids, polysaccharides, lactones and glycoside products are responsible to cause alterations in the immunomodulatory properties\(^{(28,29)}\). There are several botanical products with potential therapeutic applications because of their high efficacy, low cost and low toxicity. This will may help to new discovery and drug development.

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