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HERBAL APPETIZER LOLLYPOPS: A NOVEL DRUG DELIVERY SYSTEM FOR PEDIATRIC PATIENT

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ABSTRACT

In the present investigation, an attempt has been made to prepare and evaluate herbal appetizer Lollypops. Health problems faced by hundreds of millions of school-age children is 'anorexia' means loss of appetite. The different herbal crude drugs like tamarind, coriander, garlic, ajwon, cardamon, black pepper, ginger**,** tulsi are acts as appetite stimulants**.** The conventional dosage forms like tablets, capsules, syrups, etc. are inconvenient for pediatric patients because of difficulty to swallow tablets and capsules or unpleasant taste of the drug. As a result, the demand for developing new technologies has been increasing day by day. Lollypops are flavored herbal dosage forms intended to be sucked and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base. Herbal lollypop is designed to improve patient compliance**,** acceptability and increase oral retention time**.** All the formulations were subjected to various physicochemical evaluations like weight variation, hardness, drug content, variability, etc. Herbal lollypop can provide an attractive alternative formulation in the treatment of pediatric patients.

Keywords*:* - Herbal Lollypops, appetite stimulant.

INTRODUCTION

The loss of appetite is termed 'anorexia'. Dramatic and poorly understood alterations occur in the physiological regulation of appetite; which is then exhibited as less hunger and earlier satiety. Thus, inadequate caloric intake consequent to poor appetite can lead to malnutrition. Coates *et. al*., demonstrated that severely malnourished children often lack interest in play activities, have a decreased sense of well-being and are less able to cope with disease-related treatments. A variety of factors, both physiological and psychological, determines one's hunger, desire to eat and satiety. It is quite normal for a child up to six years of age to experience loss of appetite especially when the child is not feeling well for any reason. Hence, it is difficult to differentiate a "normal" loss of appetite from that which requires intervention. It is only when there is a weight loss or failure to gain weight that an intervention is called for. External factors such as climate, temperature, prior meals, or activity may also influence appetite· Eating behavior is regulated by a complex interplay of central neurotransmitter systems, peripheral endocrine stimuli, the circadian rhythm and environmental cues, all factors that change the behavioral state and alter homeostatic aspects of appetite and energy expenditure. Key factors driving, eating, the behavior is appetite and satiety that are regulated through different mechanisms. Brain histamine has long been considered a satiety signal in the nervous system. Studies have demonstrated that histamine blockade stimulates appetite, while increases in histamine levels suppress appetite. Serotonin (5-HT) is believed to have an inhibitory influence overfeeding behavior. Although there is compelling evidence for a serotonin (5-HT) mechanism being involved, there is considerable individual variation in response to pharmacological manipulation of 5-HT. Subtle psychological factors may also play a role in blurring the pharmacological evidence for 5-HT involvement in the highly complex activity of human feeding[7]. The first-generation antihistaminic cyproheptadine has been used therapeutically as an appetite stimulant at a dose that also appears to have antiserotoninergic activity. Appetite stimulants, although efficacious in treating malnutrition, should only be prescribed if decreased food intake secondary to inadequate appetite is the principal cause of the malnutrition and all other contributing factors have been assessed, ruled-out or treated. Pharmacological stimulants of appetite appear to be a promising intervention for anorexia. Appetite stimulants have been used to help overcome decreased appetite and malnutrition in children with various chronic illnesses. Stimulants have included cyproheptadine hydrochloride (CH), anabolic hormones and growth hormones.

Many of these have substantial side effects and may not be suitable for prolonged use. The most common adverse events reported by children taking CH included drowsiness, headache, insomnia, and dry mouth. Recent times have seen a renewed interest in herbal and other complementary therapies in the management of various chronic diseases. However, despite an increase in use, evidence for the effectiveness and safety of these complementary therapies is limited. The given formulation is a polyherbal formulation with eleven herbs that have properties to stimulate the appetite. Reasons for less appetite in babies, toddlers, and kids. According to Science, low appetite has been linked to Zinc deficiency in your body. Zinc produces hydrochloric acid which is required for proper digestion of food. A low level of Zinc produces fewer HCI which leads to poor appetite.

You can increase the levels of Zinc by providing chicken, wheat bran, cashew nuts and pumpkin seeds in your little one's diet. According to Ayurveda, the 'Pakwagni' or the fire helps us to burn the food in the tummy and convert it into energy required by the body. Indigestion, gas, and flatulence are all caused due to imbalance in this Agni. In babies and toddlers usually, the Agni or digestion process goes seemingly slow due to illnesses like fever, cold or cough. In toddlers, there can be a constant weight for about 3-4 months. Their growth has slowed down; calorie requirement is less during those months and hence low appetite results. When food is given without a proper gap of 3 to 4 hours, it won't digest properly. In such a case, the baby or toddler won't feel hungry for a long time. To overcome these problems, many marketed preparations are available in the form of chooram and syrups. By modifying these formulations in the form of lollypops which makes it more attractive to children to take such appetite stimulants. Tamarind, coriander, garlic, ajwon, cardamom, black pepper, ginger, tulsi,

MATERIALS AND METHODS

1. Extraction: The above-mentioned herbs were collected and the desired aqueous extracts were collected individually. (Tamarind, coriander, garlic, ajwon, cardamom, black pepper, ginger, tulsi).

2. Phytochemical screening: The polyherbal solution was tested to investigate different phytoconstituents present in the herbs.

3. Preparation of lollypop: It was designed to prepare candy based lollypop by heating and congealing methods using specific polymer.

Step-1: The desired quantity of sugar was discovered in the water by heating and stirring in a copper kettle until the sugar was completely dissolved. Corn syrup was added when the cooking temperature reaches 110ºC. Cooking was then continuous to 145-156^{0}C till the syrup base becomes thick.

Step-2: The finished cooked syrup (154^{0}C) was then placed in a vacuum chamber which was maintained at 274mm hg for about 30 minutes to remove the traces of water molecules and to give plasticity to the base prepared.

Step-3: The candy base was then transferred to a water-jacketed stainless steel cooling table of 214 ft. for the mixing operation. This is done manually. During the mixing cycle, the temperature of the candy base (154^{0}C) was brought to 90^{0}C to form a solidified mass. A hydrogenated vegetable oil-based lubricant was spread on the table surface to alleviate this condition. At this stage, the drug, polymers, citric acid and other excipients such as sweetening agents, flavoring agents were added manually and mixed thoroughly.

Step-4: Then this solidified mass was poured into the calibrated mold.

Step-5: Formation of the individual lollypop

Step-6: The product (lollypop) placed on the desecrater. Then the dried lollypop is then in another container and lubricated with oil so that prepared lollypops should not stick to each other.

Step-7: The prepared lollypops were packed in the aluminum foil.[19]

4. **Evaluation studies**:

Evaluation of physical properties of medicated lollypops: The formulated lollypop is evaluated for the following parameters.

a. Thickness and diameter: The thickness and diameters of the formulated lollypop were measured by using Vernier caliper.

b. Weight variation: The formulated lollypop was tested for weight uniformity. 20 lollypops were collectively and individually form the combined weight, the average weight of lollypop was determined, each lollypop weight was then compared with average weight to determine whether it is within permissible limits or not.

$$\% \text{ weight variation} = [\text{average weight} - \text{Individual weight}]\ [\text{Average weight}] \times 100$$

c. Hardness: The lollypops crushing strength, which is the force required to break the lollypop by compression in the diametric direction was measured in triplicate using Pfizer tablet hardness tester.

d. Friability: the Roche friability test apparatus was used to determine the friability of the lollypops. Pre-weighted lollypop was placed in the apparatus, which was subjected to 100 revolutions. Then the lollypop was reweighed. The percentage friability calculated was using formula. [29]

$$\%\text{friability} = [\text{Initial weight} - \text{Final weight}] \times 100$$

e. Drug content: lollypop dissolved in 100 ml distilled water and sonicated 30 minutes and filtered from the above solution 1ml was taken in the volumetric flask and diluted up to 10 ml (100µg/ml) and it has analyzed by spectrophotometer against appropriate blank.

f. Moisture content: The sample was weighed and crushed in a mortar. From this, one gm of the samples was weighed and placed in desiccators for 24 hours. After 24 hours the sample is weight accurately. The moisture content is determined by the abstracting of the final weight from the initial weight of lollypops.

g. Disintegration test: disintegration study performed by disintegration apparatus. Put one lollypop into each tube suspend the assembly in the beaker containing pH 6.8 phosphate buffer and operate without the disc 30 min remove the assembly from the liquid. The lollypop pass.

h. *In vitro* drug release: In-vitro release studies were performed using USP apparatus II (paddle type). The dissolution test was performed by using 900 ml of phosphate buffer (pH 6.8) 37±0.5^{0}C, at 50rpm. The samples (5 ml) were collected at a predetermined time several time intervals and replaced with an equal volume of fresh medium and analyzed using UV-

visible Spectrophotometer. Drug concentration was calculated from a standard calibration of and expressed as a cumulative % drug release.

i. Anti-microbial assay: 100 mg of the polymer sample were separately aseptically mixed with 9ml of sterile normal saline and pH adjusted to 7.1ml of each dispersion was mixed 20ml of sterile lactose broth and placed separately in Petri dish. And the plates were incubated 37±1^{0}C for 24hr. After the incubation period, the samples were observed for the presence of microflora.

j. Taste masking test: first the stability studies 10 healthy volunteers would be given to taste standard quinine solution (120-160mcg/ml) .by swirling the solution in the buccal cavity for 30sec. and spitting out the solution volunteers would be asked to rank them a bitterness scale (rank 15) after 30min, these volunteers would be asked to evaluate the taste of drug lollypop in the same manner and compare on the same scale. [30]

k. Stability study: stability studies for the lollypop were carried out at 40^{0}C at 75%RH for 90 days. For every 15 days, the parameters like, drug content, weight variation, color, hardness, and moisture content were determined.[28]

Table No. 1: Evaluation test

Sr. No.	Name of evaluation test	Procedure
1.	Thickness	Thickness and diameter measured by using a Vernier caliper
2.	Weight variation	% weight variation = [average weight− Individual weight] [Average weight] × 100
3.	Hardness	Hardness was measured in triplicate using a Pfizer tablet hardness tester.
4.	Friability:	% friability = [Initial weight –Final weight]×100
5.	Drug content	It has analyzed by spectrophotometer
6.	Moisture content	The moisture content is determined by the abstracting of the final weight from the initial weight of lollypops.
7.	Disintegration test	Disintegration study performed by disintegration apparatus
8.	In vitro drug release	In-vitro release studies were performed using USP apparatus II (paddle type)
9.	Antimicrobial assay	The final prepared samples were observed for the presence of microflora.
10.	Stability study	Stability studies for the lollypop were carried out at 40^{0}C at 75%RH for 90 days

RESULTS AND DISCUSSION

In the present study, an attempt was made to develop herbal appetizer lollypop. Formulations were subjected to various parameters such as weight variation, thickness, diameter, hardness, drug content, friability, and in-vitro dissolution study. Stability studies were performed at 40℃ at 75%RH for 32 days. All the formulations showed a good physical appearance. The weight variation was found to be in the range of 4.92±0.06gm to 5.05±0.02gm. Thickness was found to be in the range of 7.30±0.00mm to7.46±0.05mm whereas diameter was found to be 2.74±0.00cm which is uniform for all formulations. The results of weight variation, thickness and diameter were depicted in below Table.

Table No. 2: Evaluation Parameters of herbal appetizer lollypop

Parameters	**F0***	**F1***	**F2***	**F3***
Weight variation(gm)	4.93±0.06	4.92±0.06	5.02±0.07	5.05±0.02
Thickness(mm)	7.33±0.05	7.30±0.00	7.46±0.05	7.33±0.05
Diameter(cm)	2.74±0.00	2.74±0.00	2.74±0.00	2.74±0.00
Hardness(kg/cm2	10.1±0.15	10.1±0.20	10.2±0.23	11.3±0.11
% Drug content	98.20±0.85	97.23±0.35	97.66±0.47	97.80±0.26
% Friability	0.45	0.23	0.28	0.31

*F0, F1, F2, F3 are time intervals which are evaluated for 32 days

Hardness was found to be in the range of 10.1±0.15kg/cm2to 11.3±0.11kg/cm2 whereas the percentage friability of all formulations was found to be in the range of 0.23% to 0.45% which was found to be well within maximum 1% limit. The results of hardness and friability indicated that the lollypops are mechanically stable. The drug content was found to be in the range of 97.23±0.35% to 98.20±0.85% which is within the acceptable range as specified in Indian Pharmacopoeia (95%- 105%). The results of hardness, friability and drug content showed in the above Table.

CONCLUSION

From the above investigation, it is concluded that herbal drugs like Tamarind, coriander, garlic, ajwon, cardamom, black pepper, ginger, tulsi, can be used to formulate effective

herbal appetizer lollypop. This will offer better pediatric compliance and innovative dosage form.

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