Indian Journal of Drugs, 2019, 7(2), 73-80 ISSN: 2348-1684

Research Article

FORMULATION AND EVALUATION OF MEDICATED CANDY CONTAINING ALBENDAZOLE FOR PEDIATRIC

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Received: 28.02.2019
Accepted: 22.06.2019

Access this article online

Website:
www.drugresearch.in

Quick Response Code:

ABSTRACT

There are several dosage forms in the market; there is a need for more dosage form which acts effectively and locally as well as systematically. The benefits of the research work are increased retention time of the oral cavity and increased bioavailability, reduction in gastric irritation by passing first pass metabolism. Candy are flavored medicated dosage form intended to be sucking and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base. Medicated candy is designed to improve patient compliance, acceptability. The candy was prepared by heating and congealing method using methylcellulose, citric acid as polymer. Drug albendazole is an anthelminthic drug which contain very bitter taste drug. For patient acceptability we need to improve the taste of the drug by different saccharides like sucrose, dextrose. Pourability, Texture and Elasticity is improved by different plasticizers like glycerin. It was found that the formation containing methyl cellulose and combination of saccharides like dextrose, sucrose showed better drug release and it was more stable, unlike the other formulation.

KEY WORDS: Medicated candy, albendazole, heating and congealing Method, Saccharides, Plasticizers.

INTRODUCTION

Oral dosage forms vary and have advantages over other dosage forms. They are economical and safe to the patient. Their toxicity is delayed due to the onset of action which permits easier recovery than in case of other dosage forms1. A drug can be administered via a many different routes to produce a systemic pharmacological effect. The most common method of drug administration is via per oral route in which the drug is swallowed and enters the systemic circulation primarily through the membrane of the small intestine. The oral route of drug administration is the most important method of administering drug for systemic effect. Absorption of drugs after oral administration may occur at the various body sites between the mouth and rectum. A drug taken orally must withstand large fluctuations in pH as it travels along the gastrointestinal tract, as well as resist the onslaught of the enzymes that digest food and metabolism by micro flora that live there. Difficulty is experience in particular by paediatric and geriatric patient, but it also applies to people who are ill bedridden and to those active working patients who are busy or travelling, especially those who have no access to water. In these cases, oral mucosal drug delivery is most preferred. The buccal and sublingual routes of administration can be utilized to bypass the hepatic first-pass elimination of drug. Within the oral mucosal cavity. The buccal region offers an attractive route of administration for systemic drug delivery.2

Physiology of the Oral Mucosa 2,3,4,5

Structure: The main difference between the oral mucosa and skin as compared to the gastrointestinal (GI) tract lining lies in the organization of the different epithelia. Within the oral cavity the

masticatory mucosa has a keratinized or cornified epithelium, and covers the stress-enduring regions such as the gingival and the hard palate , proving chemical resistance and mechanical stength. It is divided into four layers:keratinized , granular , prickle-cell , and basal layer (Figure 1)

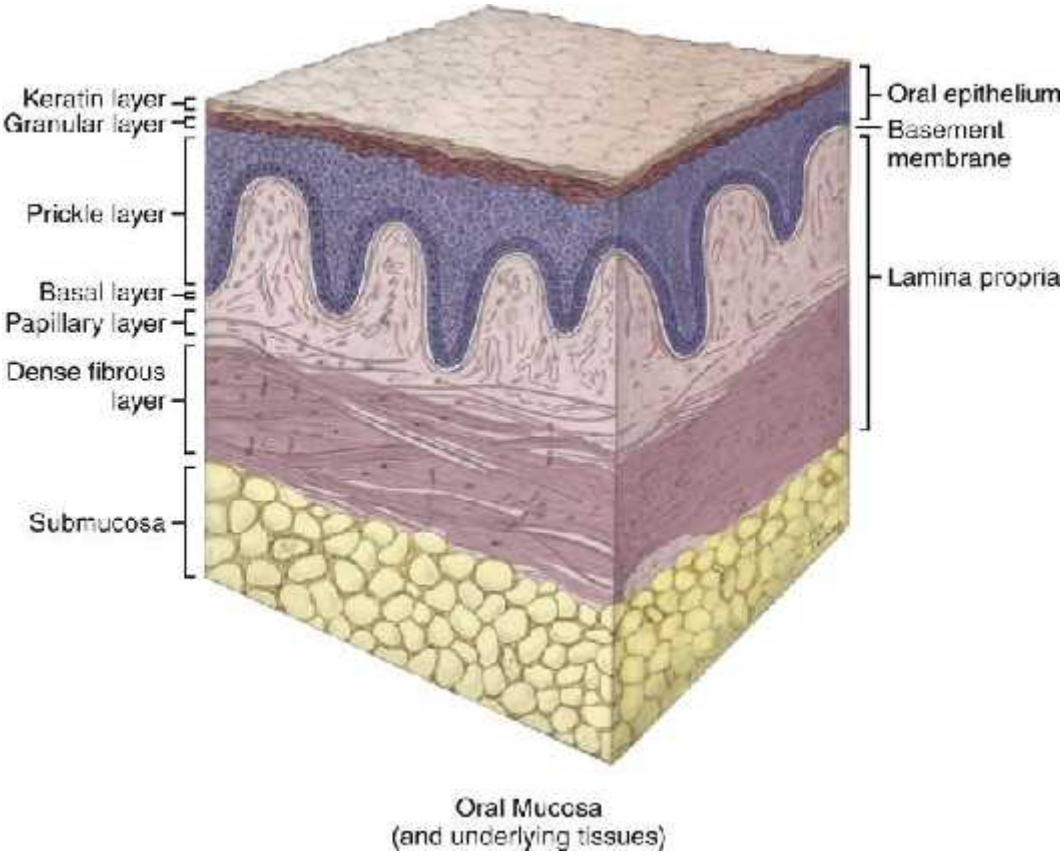


Figure No. 1.1; STRUCTURE OF THE MUCOSA

The lining mucosa, which provides elasticity, in contrast, is comprised of non-cornified surface epithelium covering the rest of the regions including the lips, cheeks, floor of the mouth, and soft palate. It also can be further divided into superficial, intermediate, prickel - cell, and basal layer. The third type of mucosa is the specialized mucosa consisting of both keratinized and non-keratinized layers, and is restricted to the dorsal surface of the tongue. The intercellular spaces contain water, lipid, and proteins.

Dosage forms (6,7)

A) Lozenges

Lozenges can be used as an alternative dosage form to tablets and capsules when patients are unable to swallow. Though the lozenges usually dissolve in about 30 min, the patient control the rate of dissolution and absorption because the patient sucks on the lozenge until it dissolves. Increase in the amount of sucking and production of saliva may also lead to increased dilution of the drug and often accidental swallowing.

B) Tablets

A tablet is a pharmaceutices dosage form.Tablets may be defined as the solid unit dosage form of medicament or medicaments with or without suitable exicipents and prepared either by molding or by compression.It comprises a mixture of active substances and exipients, usually in powder form, pressed or compacted from a powder into a solid dose.The excipients caninclude diluents, binders or

granulating agents, glidants(flow aids) and lubricants to ensure efficient tableeting;disintegrants to promate tablet break-up inthe digestive tract ;sweeteners or flavour to enhance taste; and pigments to make the tablets visually attractive or aid in visual O of an unknown tablet. A polymer coating is often applied to make the tablet smoother and easier to swallow, to control the release rate of the active ingredient, to make it more resistant to the environment (extending its shelf life), or to enhance the tablet's appearances.

Advantages of Oral Mucosal Drug Delivery system (1)

1. Bypass of the gastrointestinal tract and hepatic partake system, increasing the bioavailability of orally administered drug that otherwise undergo hepatic first-pass metabolism. In addition, the drug is protected from degradation due to pH and digestive enzyme of the middle gastrointestinal tract.
2. The large contact surface of the oral cavity contributes to rapid and extensive drug absorption.
3. Oral mucosal delivery occurs is less variable between patients, resulting in lower inter-subject variability as compared to transdermal patches.
4. Improved patient compliance due to the elimination of associated pain with injections; convenience of administration as compared to injections or oral medication.
5. Sustained drug delivery.
6. A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued.
7. Increased ease of drug administration.
8. In comparison to TDDS, mucosal surface does not have a stratum conneum. Thus, the major barrier layer to transdermal drug delivery is not a factor in oral mucosal routes of administration. Hence oral mucosal systems exhibit a faster initiation and decline of delivery than do transdermal patches.
9. Though less permeable than the sublingual area, the buccal mucosa is well vascularized, and drugs can be rapidly absorption into the venous system underneath the oral mucosa.

Limitation of Oral Mucosa Drug Delivery System (1)

For local action the rapid elimination of drug due to the flushing action of saliva or the ingestion of foods stuffs may lead to the requirement for frequent dosing. The non-uniform distribution of drug within saliva on release from a solid or semisolid delivery syatem could mean that some areas of the oral cavity may not receive effective levels. For both local and systemic action, patient acceptability in terms of taste, irritancy and 'mouth feel' is an issue. For systemic delivery the relative impermeability of oral cavity mucosa with regard to drug absoption, especially for large hydrophilic biopharmaceuticals, is a major concern.

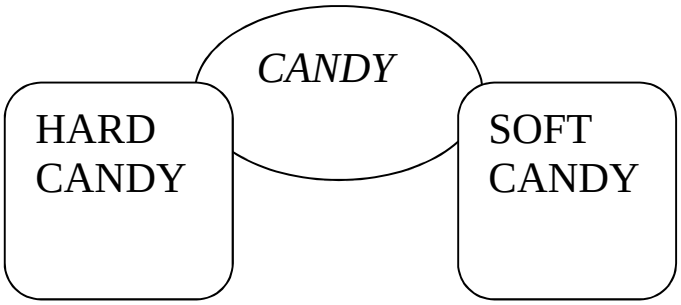
Medicated candy

Candy are solid dosage form, containing medicament in a sweetened and flavored base, intended to dissolve slowly in the mouth. candy is mainly contain sweetening agent, flavoring agent, colouring agent, opacifiers and stabilizing agent. Candy are used for patients who cannot swallow solid oral dosage form.[17] Oral administration is the most popular route due to ease of ingestion, pain avoidance and most importantly patient compliance. As a result, the demand for developing new technologies has been increasing day by day. [18]

General consideration for designing medicated candy

There are mainly drug dosage forms like lozenges, tablet, inhalers, and syrups, are in markets for the treatment of the same. These preparations are commonly used for the purpose of local effect or systemic effect.

TYPE OF CANDY



Hard candy

Hard candy might be considered solid syrups of sugars. These dosage forms are made by heating sugars and other ingredients together and then pouring the mixture into a mold. So water is evaporated off by boiling the sugar mixture during the compound process. Hard candy are mixtures of sugar and other carbohydrates in an amorphous(non-crystalline) (or) glassy condition. Hard candy should not disintegrated but instead provide a slow, uniform dissolution (or) erosion over 30 minutes. A hard candy, or boiled sweet, is a sugar candy prepared from one or more sugar-based syrups that is boiled to a temperature of 160℃(320°F)to a make candy.

Soft candy

Soft candy have become popular because of easy with they can be extemporaneously prepared and their applicability of a wide variety of drugs. The base usually consist of a mixture of various PEGs, acacia (or) similar materials glycerol gelatin (or) an acacia: sucrose base. These candy may be coloured and they can be either slowly dissolved in the mouth (or) chewed, depending on the intended effect of the incorporated drug.

Preparation of candy

It was planned to prepare candy based candy by heating and congealing method using specific polymer. Required quantity of sugar syrup was prepared mixing and water. Dextrose was dissolved in small quantity of water and heated it to110℃ till dextrose dissolves completely forming as clear viscous syurp. Then the dextrose syrup was poured into the sugar syrup and heated to 160℃ till the colour changes to Golden yellow. Flavour was added between 120℃ to 135℃ then temperature was bought down to 90℃ and drug, polymer and other ingredients were added and mixed it well. The prepared mixture was pured into the calibrated mould and kept it for air dry for1-2 hrs. The prepared candy were stored wrapped in aluminum foil and stored in desiccators to prevent moiture uptake.

Formulation of medicated Candy

Ingredients Examples

1) Candy base :

a. Sugar : Dextrose,sucrose.

b. Lubricants : Glycerine.

c. Binders : methylcellulose.

d. Colouringagents :Bixa.

e. flavouring agent : pineaapleflavour.

Evaluation test of candy (17,23)

1. Weight variation

Candy was randomly checked to ensure to that uniform weight candy were being made. 20 candies Formulation, weight individually and average weight and % weight variation was calculated. The requirements are met if the weights of not more than 2 of the candy differ from the average weight by more than the percentage listed in the accompanying table and no candy differs in weight by more than double that percentage.

2. Thickness

Thickness was measured using Vernier Calipers. It was determined by checking the thickness of ten candy of each formulation. The extent to which the thickness of the each candy deviated from ±5% of the standard value was determined.

3. Hardness

Hardness indicates the ability of a tablet to withstand mechanical shock while handling the hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. There tablets were randomly picked and hardness of the tablets was determined.

4. Drug content

The drug content was estimated for all the formulations of Medicated lozenges. Lozenges from each batch were selected and weighed individually and crushed in a mortar. The resultant powder was dispersed in dimethyl formamide solvent and the final volume was then made to 100ml using pH 6.8 buffers. The solution in the volumetric flask was filtered, diluted suitably, and analyzed spectrophotometrically at 295 nm using UV-visible double-beam spectrophotometer (Lab India).

5. Friability (F)

Roche Friabilator was used for testing the friability. Twenty tablets were weighted accurately and placed in the tumbling apparatus that revolves at 25 rpm. After 4 min., the tablets were weighted and the percentage loss in tablet weight was Determined.

$$F=Wintial-Wfinal/Wintial\times100$$

Disintegration test

This was carried out for soft lozenges. The disintegration time of lozenges were determined using USP Disintegration apparatus and disintegration time was noted in pH 6.8 phosphate buffer.

Advantage of medicated candy (20)

1. Candy can be given to those patients who have difficulty in swallowing.
2. Keeping the drug in contact with the oral cavity for an extended period of time.
3. It has a pleasant taste and it extends the time that a quantity of drug remains in the oral cavity to elicit a therapeutic effect also, pharmacist can prepare candy extemporaneously with minimal equipment and time.
4. Easy to prepare with minimum amount of equipment and time.
5. Do not require water intake for administration. Technique is non-invasive, as is the case with parentral.

Disadvantages of medicated candy

1. Heat labile drug cannot be used in this formulation because of the high temperature required for preparation.
2. Drug having minimum bitter taste are suitable.
3. Heat stable drug are suitable.

Objective-

1. To fabricate medicated tablet lozenges for anthelminthic.
2. To formulate an alternative dosage from for pediatric patient.
3. To improve patient compliance and acceptance.
4. To achieve maximum drug efficacy.

MATERIALS AND METHODS

Melting point determination

Melting point of drug determined using Thiele's tube- capillart method. Albendazole drug was found in the range of 208-210°C

Preparation of candy

It was planned to prepare candy based candy by heating and congealing method using specific polymer.

Sr .No	Ingredient	Formula	Formula
1	Albendazole	0.2 gm	0.2 gm
2	Sucrose	3gm	3gm
3	Dextrose	1.5gm	1.5gm
4	Methyl Cellulose	0.1gm	0.1gm
5	Citric acid	0.12gm	0.12gm
6	Glycerin	3%	4%

Table NO.1. Formula for Candy

Required quantity of sugar syrup was prepared mixing and water. Dextrose was dissolved in small quantity of water and heated it to110^{O}C till dextrose dissolves completely forming as clear viscous syurp. Then the dextrose syrup was poured into the sugar syrup and heated to 160^{0}C till the colour changes to Golden yellow. Flavour was added between 120^{0}C to 135^{0}C then temperature was bought down to 90^{0}C and drug, polymer and other ingredients were added and mixed it well. The prepared mixture was pured into the calibrated mould and kept it for air dry for1-2 hrs. The prepared candy was stored wrapped in aluminum foil and stored in desiccators to prevent moiture uptake.

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6.Disintegration test

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RESULTS

Melting point determination

Melting point of Albendazole was found in the range of 206^0-208^oC which is in the reported range that is 208^0-210^oC indicated absolute purity of drug sample.

Characterization of formulation

Table no.2 Evaluation parameter

PARAMETER	F_1	F_2
Weight variation(%)	4.72±0.02	4.40±0.02
Thickness (mm)	15.1±0.02	14.1±0.02
Hardness (kg/cm^2)	10.7±0.11	10.1±0.11
Drug content	98.46±0.21	97.50±0.21
Friability (F)	0.26	0.23
Disintegration time(sec.)	30	28

CONCLUSION

In the present study, an attempt was made to formulate and evaluate candy based medicated candy of albendazole for the treatment of anthelmintic. Candy based medicated candy of albendazole was prepared by Heating and congealing method. In this study, formulation was developed using Methyl cellulose, sucrose, dextrose. Evaluation parameters like thickness, weight variation, hardness show that they were within the limits. Drug content uniformity was also found to be within the limit. The formulation containing plasticizers are improving the texture, elasticity and portability of the candy. Concluded that glycerine plasticzer 3% shows better looking properties of medicated candy. Hence it may be considered as preferred formulation.

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