Formulation and Evaluation Of Salbutamol Sulphate Lollipops

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Abstract: Cough is a prevalent medical concern, often leading to numerous clinical visits and referrals. Despite its ubiquity, there's a lack of objective tools to measure and quantify cough, complicating its evaluation. This paper elucidates the intricate mechanisms underlying cough reflex and its association with various clinical conditions. Additionally, it explores the potential of lollipops as a novel drug delivery system, particularly for patients with swallowing difficulties or aversions to conventional formulations. Salbutamol Sulphate, a common bronchodilator, was formulated into lollipops and subjected to rigorous evaluation, including preformulation studies, organoleptic characterization, physical parameter assessments, in vitro dissolution studies, and stability assessments. The results demonstrated promising characteristics of the prepared lollipops, including satisfactory organoleptic properties, uniformity in thickness and diameter, acceptable weight variation, appropriate hardness, controlled drug release profile, and stability under various conditions. Overall, this research underscores the potential of lollipops as a patient-friendly dosage form for managing cough and highlights the importance of innovative drug delivery systems in enhancing patient compliance and therapeutic outcomes.

Keywords: Salbutamol Sulphate, Cough, Lollipops, Pediatric

I. INTRODUCTION

Cough is one of the most common medical complaints accounting for as many as 30 million clinical visits per year. Up to 40% of these complaints result in a referral to a pulmonologist. A cough is an innate primitive reflex and acts as part of the body's immune system to protect against foreign materials. Coughing is associated with a wide assortment of clinical associations and etiologies. Furthermore, there are no objective tools to measure or clinically quantify a cough. This activity reviews the workup of an unexplained cough and highlights the role of the interprofessional team in evaluating and improving care for patients with cough. Cough is a protective mechanism resulting from a complex reflex initiated by the activation of irritating receptors in the airway constituting a forced expulsion maneuver, usually against a closed glottis. [1, 2]

Cough is a natural defense mechanism that along with mucociliary clearance, bronchoconstriction and phagocytosis can effectively protect the respiratory tract from inhaling foreign bodies and by clearing excessive bronchial secretions. Cough may be a voluntary act or a spontaneous reflex arc and, in this case, involves receptors, an afferent pathway, a center processing information, an efferent pathway and effectors. The receptors are placed throughout the bronchial tree and, although in a lesser extent, also in other areas: ear, paranasal sinuses, pleura, diaphragm, pericardium and esophagus. [3]

II. MECHANISM OF ACTION OF COUGH

Cough is normally produced through the stimulation of sensory receptors of the glossopharyngeal and vagus nerves, innervating the mucous membranes of the lower pharynx, larynx, trachea, and smaller airways of the respiratory system.

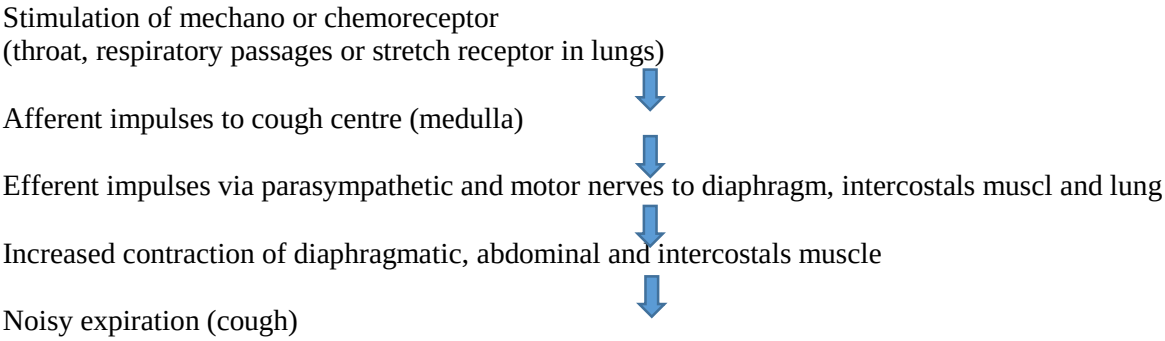


Fig. No. 1 Mechanism of Action of Cough

The most common cause of chronic dry cough is a group of related conditions of chronic rhinitis, sinusitis, and postnasal drip. In these cases the cough reflex may be sensitized through an action of inflammatory mediators from the nasal mucosa on the airways or a reflex sensitization of airway sensory nerves.

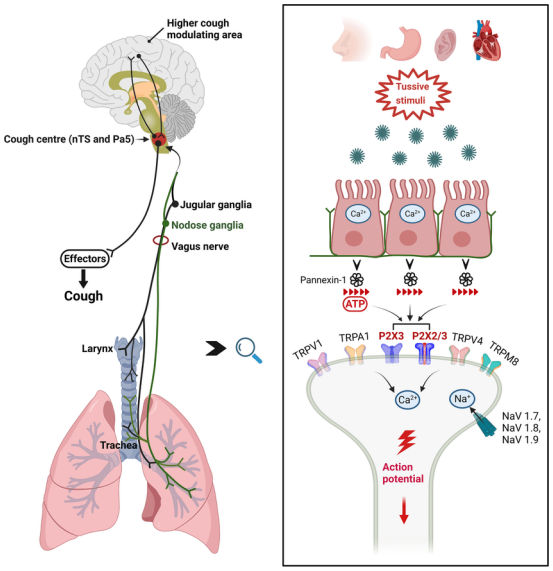


Fig. No. 3: Mechanism of cough

III. LOLLIPOPS:-

The administration of drugs through oral route is the most common and the easiest way of administering a drug. Oral route of drug administration has been widely acceptance up to 50-60% of total dosage form. Solid dosage form provides ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. However, pediatrics, geriatric and bedridden patient shows inconvenience swallowing conventional tablets or capsules due to difficulties in swallowing with lesser amount of water with the medication, unable to tolerate the taste of many drug when formulated as liquid dosage form, resulting in poor patient compliance. [4]

For the past two decades, there has been an enhanced demands for more patient compliance dosage form. As a result, the demand for their technologies has been increasing three-fold annually. Since the development cost of a new chemical entity is very high, the pharmaceutical companies are now focusing on the development of new drug delivery system for existing drug with an improved efficacy and bioavailability together with reduced dosing frequency to minimize side effects. [5, 6]

A. Types of lollipops

❖ Hard Lollipops (7)

Hard lollipops might be considered solid syrups of sugar. These dosage forms are made by heating sugars and other ingredients together and then pouring the mixture into a mould. Hard lollipops are similar to hard candy. In fact, many hard lollipops formulas are modification of hard candy formulas. The dosage form needs low mixture content. So water is evaporated off by boiling the sugar mixture during the compound process. Hard candy lollipops are mixtures of sugar and other carbohydrates in an amorphous glassy condition. These lollipops can be considered solid syrups of sugars and usually have a moisture content of 0.5%-1.5%. Hard lollipop should not disintegrate but instead provide a slow, uniform dissolution erosion over 30 min.

❖ Soft Lollipops (8)

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

❖ Advantages of lollipops (9)

- Lollipop improve patient compliance, acceptability.
- Lollipops can be given to those patients who have difficulty in swallowing.
- Lollipops have a pleasant taste and it extends the time that a quantity of drug remains in oral cavity to produce therapeutic effect.
- Lollipops extends the time of drug in oral cavity to elicit the specific effect.

- Lollipops are early to prepare with minimum amount of equipment and time.
- Do not require water intake for administration.
- Technique is non-invasive and it is the case with parenteral.

❖ **Disadvantages of lollipops (9)**

❖ • Heat labile drugs cannot be used in this formulation because of the high temperature required for preparation.

❖ • Drugs having minimum bitter taste are suitable.

❖ • Heat stable drugs are suitable.

❖ • Draining of drug from oral cavity to stomach along with saliva.

IV. MATERIAL AND METHODS

A. Material used:

Salbutamol Sulphate Gift Sample from Orex Pharma Pvt. Ltd Dombivli, Maharashtra, India. Loba Pvt. Ltd, MumbaiLtd in Mumbai provided all of the remaining ingredients.

B. Preparation of Medicated Lollipops:

Syrup base was prepared by dissolving 66.66% w/v sucrose in purified water at 110 °C and continue stirring for about 30 min. Scaled down time to appropriate with the quantity of material used was notice.

C. Preparation of medicated lollipops:

Medicated lollipops of 5 g was prepared by heating and congealing technique. The base was prepared in a beaker dissolving sucrose in the water while heating and stirring at 110°C for about 20 min, followed with corn syrup addition and stirring continued for 30 min, while raising the temperature to 160 °C. The material will left to cool, and the temperature was brought down 90°C till a semi-plastic mass obtained. Drug, polymer, coloring, and flavoring agents added and mixed the materials for 10 min. After mixing all the ingredients the mixture will poured into silicone molds that had a diameter of 3 cm and 6 mm thickness, then it was wrapped with aluminum foil and left to solidify at room temperature. The ideal time of this step was determined by taking a small amount of the mixture using a glass rod and placed it in the beaker containing water would transfer to the solid-state directly at this moment the mixture will poured into silicone molds.

D. Formulation of herbal lollipops:

Table 1: Formulation of Salbutamol Sulphate lollipop

Sr.no	Composition	F1	F2	F3	F4	F5
1	Salbutamol sulphate(mg)	2	2	2	2	2
2	Sucrose (g)	4.6	12	12	10	9
3	Dextrose (g)	0.1	0.12	0.12	0.30	0.50
4	HPMC (g)	0.1	0.12	0.12	0.30	0.50
5	Citric Acid	0.1	0.1	0.1	0.1	0.1
6	Corn syrup (g)	1	1.66	2.5	2.5	3
7	Calcium Carbonate(g)	-	1.4	1	1	1
8	Coloring agent (g)	Q. S	Q. S	Q. S	Q. S	Q. S
9	Flavoring agent (g)	Q. S	Q. S	Q. S	Q. S	Q. S
10	Purified water	Q. S	Q. S	Q. S	Q. S	Q. S
	Total (g)	15	15	15	15	15

V. RESULT AND DISCUSSION:

A. PREFORMULATION STUDIES

a) Physical Characteristics

Salbutamol sulphate was checked for its colour, odour and texture. Solubility test for salbutamol sulphate was carried out in different solvents such as Ethanol, water, chloroform, phosphate buffer and result are shown in table No. 2.

Table No. 2: Physical characterization of drug

Properties	**Observation**
Colour	White
Odour	Odourless
Taste	Tasteless
Solubility	Soluble in water, ethanol Buffer
Nature	Crystalline

b) Melting point Determination

The average melting point of salbutamol sulphate was found to be 180.33^{0}C. It was found to be within reported range (180^{0}C) of the drug and therefore its compliance with the standard value

Table No. 3: Melting point of salbutamol sulphate

Melting Point (°C)	**Average Melting Point (°C)**
179 181 181	180.33

c) Determination of λ max

The subsequent solution was then examined in the range of 200 and 400 nm with an UV- spectrophotometer. The UV range was recorded and the most elevated worth acquired with the authority monograph's UV range. Determination of wavelength (λ_{max}) of Salbutamol Sulphate was obtained by scanning the Distilled Water stock solution. The maximum Wavelength result are shown in table 4.

Table No. 4: Wavelength maximum (λ max) of Salbutamol Sulphate

Drug	**λ max**	
	Standard Value Of λ max	**Observed Value of λ max**
Salbutamol Sulphate	276 nm	276 nm

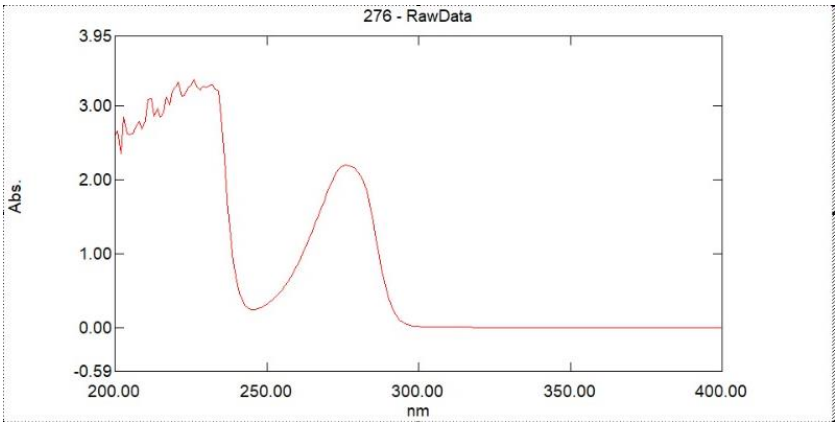


Fig. No. 2: λ Max of Salbutamol Sulphate

d) Construction of Calibration Curve of Salbutamol Sulphate

The maximum absorption of Salbutamol Sulphate was found to be at 276nm and hence it is selected as the wavelength for further studies.
In the calibration curve, linearity was obtained between 10-50 µg/ml concentration of Salbutamol Sulphate and regression value was found to be **R^2= 0.9732.** Hence we can conclude that Salbutamol Sulphate obeys Beer Lamberts law at the concentration between 10- 50 µg/ml. The result are shown in Table. 5 and figure 3.

Table No. 5: Concentration and Absorbance values of Salbutamol sulphate

Sr. No	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.013
3	20	0.113
4	30	0.211
5	40	0.310
6	50	0.415

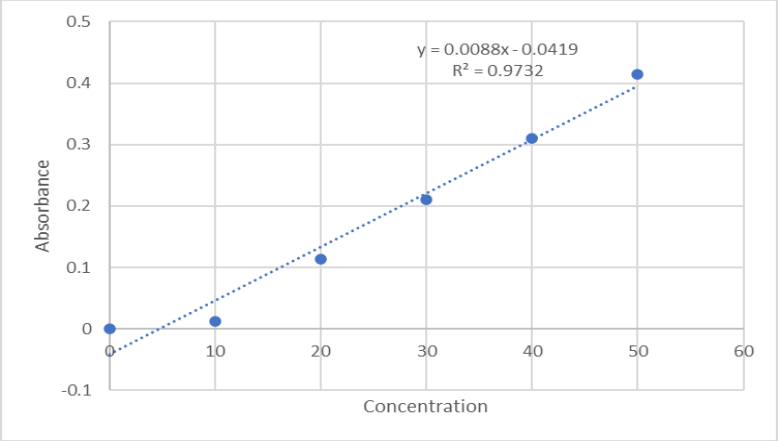


Fig. No. 3: Calibration curve of salbutamol sulphate

e) **FTIR Spectroscopy:**

IR of Salbutamol was carried out in Fourier transform infrared spectroscopy (schimadzu). About 1 mg of drug was dispersed in KBr powder and kept in sample holder and FTIR spectra was obtained by powder diffuse reflectance on FTIR spectrophotometer.
It showed characteristic peaks of OH at 3317.3 cm^{-1}, peak of NH at 3555.9 cm^{-1}, peak of CH at 2933.4 cm^{-1}.

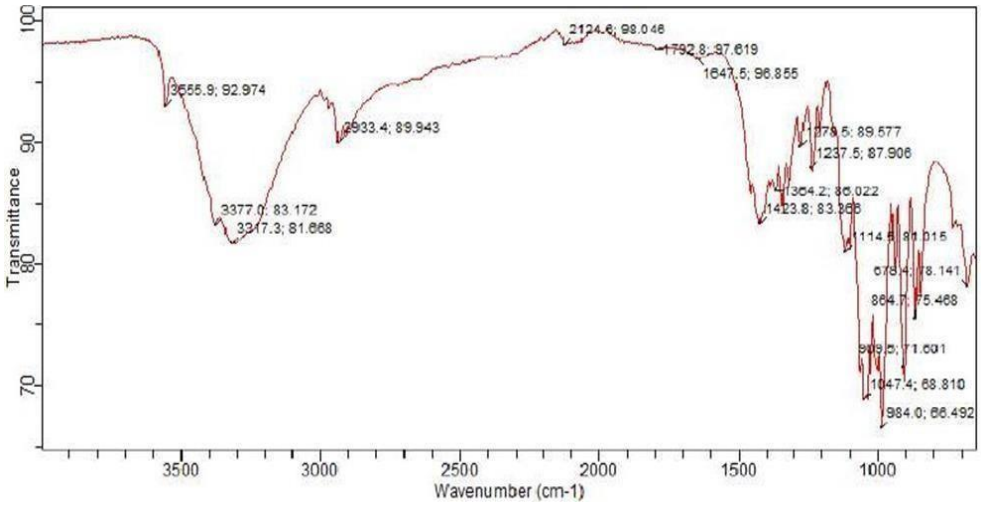


Fig. No. 4: FTIR Spectra of Salbutamol

Compatibility of drug with excipient (Sucrose, HPMC, Citric acid, Calcium Carbonate) was studied by FTIR. The FTIR spectra of all excipient with pure drug shows the characteristic peaks same as that of pure drug and slightly shift in peak values when compared with the characteristic peak values of pure drug. The IR spectra of the entire sample showed the prominent characterizing peak of pure drug which confirmed that no chemical modification of the drug had been take place.

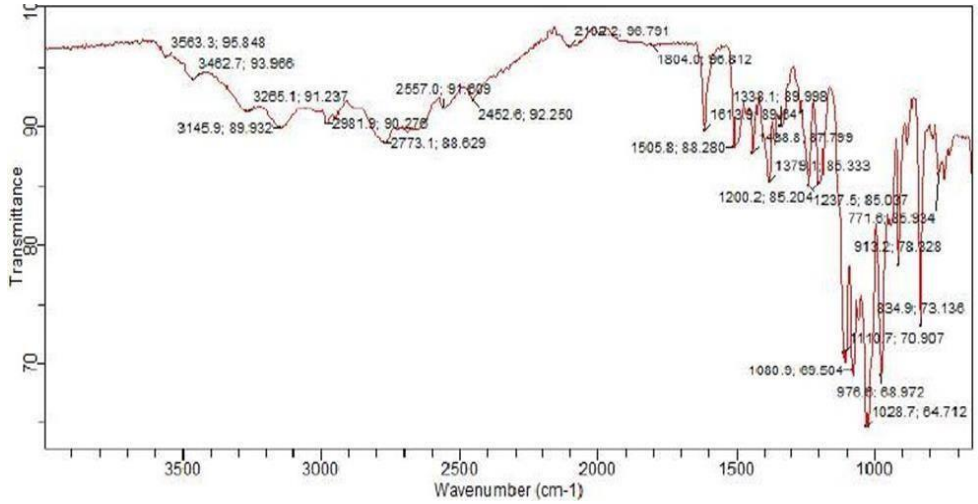


Fig. No. 5: FTIR spectra of Drug with Excipient

B. EVALUATION OF MEDICATED LOLLIPOPS

a) Organoleptic Characterization

The prepared lollipops were inspected visually for colour, presence of any particularly materials and texture. This test is important regarding patient compliances and acceptance.

Table No. 6: Organoleptic Characteristics of Lollipops

Formulation	Colour	Clarity	Presence of any particular materials	Texture
F1	Orange, very sticky	Homogeneous	No	Satisfactory
F2	Orange, Sticky, Easily Removed from mould, smooth	Homogeneous	No	Satisfactory
F3	Orange, Sticky, Smooth	Homogeneous	No	Good

F4	Orange, Sticky,	Homogeneous	No	Very Good
F5	Orange, little Sticky,	Homogeneous	No	Very Good

b) Thickness and Diameter

Diameter of the lollipop is important for uniformity of lollipop size. Thickness and diameter was measured using Vernier Calliper. And the result obtained as shown in Table 7.

Table No. 7: Thickness and Diameter of Lollipops

Formulation	**Thickness in mm**	**Diameter in cm**
F1	12.80	3
F2	13	3.1
F3	13	3.1
F4	13	3.1
F5	13	3.1

c) **Weight Variation Test for Lollipops**

Taken the individual weight of the 20 lollipops in weighing balance and taken out the average weight of the 20 lollipops. And result as shown in Table 8.

Table No. 8: Weight variation of Lollipops

Formulation	**Weight Variation of Lollipops in g**
F1	15.30
F2	15.63
F3	15.45
F4	15.33
F5	15.48

d) Hardness test of lollipops:

The resistance of lozenges to shipping or breakage under conditions of storage transportation and handling before usage depends on its hardness. The hardness of lollipops can be measured by using Monsanto Hardness tester. Measures force required to break the lollipop and hardness was measured in terms of kg/cm^2.

Table No. 9: Hardness of Lollipops

Formulation	**Hardness in kg/cm^2**
F1	10.85
F2	11.00
F3	10.80
F4	11.04
F5	11.08

e) Moisture Content:

1 g of the sample was weighed and placed in desicators for 24 hr. After 24 hour the sample is weighed. The moisture content is determined by substracting the final weight from the initial weight of the sample of lollipops.

Table No. 10: Moisture Content of Lollipops

Formulation	Initial Weight of Lollipop (gm)	Final Weight of Lollipop (gm)	% Moisture Content
F1	1	0.60	40
F2	1	0.66	34
F3	1	0.71	29
F4	1	0.75	25
F6	1	0.81	19

f) In-Vitro Dissolution Studies:

Dissolution rate was studied using USP-II paddle dissolution apparatus, in 900 ml of salbutamol sulphate 37±0.5°C at 100 rpm.

Table No. 11: In-vitro dissolution studies

Sr. No.	Time (Min)	% Drug Release				
		F1	F2	F3	F4	F5
1	5	25.2	28.1	31.5	38.4	37.32
2	10	26.7	31.5	35.4	50.2	51.11
3	15	29.5	35.3	39.3	56.9	60.8
4	30	27.1	36.9	43.4	63.5	68.5

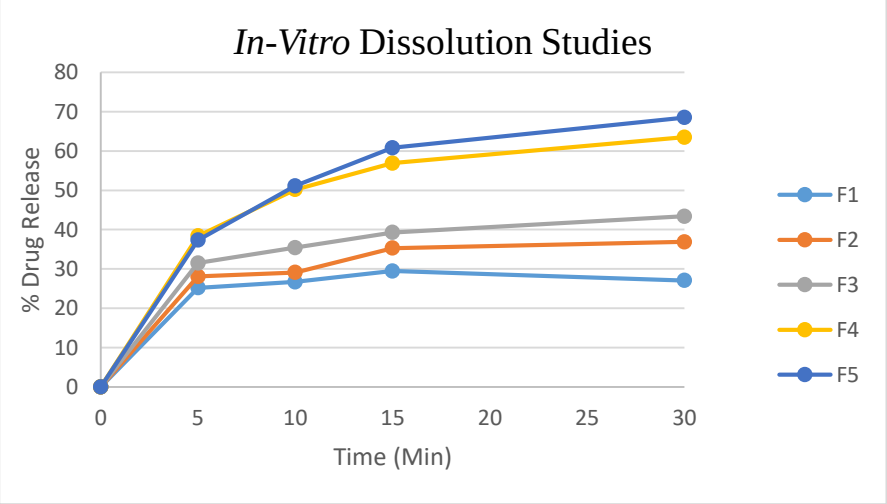


Fig. No. 6: In-Vitro Drug Release

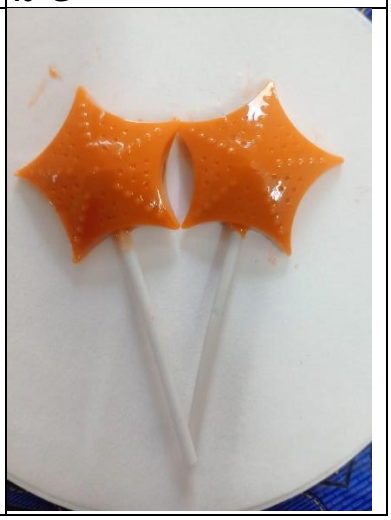
g) **Stability Study:**

The stability test was carried out for one month and results revealed that all the lollipops showed better stability at 8^0C, Room Temperature and 40^0C.

Table No. 12: Stability study of Lollipop

Days	Temperatures	Colour	Crystallization	Presence of any particular materials
8	8^0C	Reddish, little Sticky	No	No
	Room temp.	Reddish	No	No
	40^0C	Reddish, sticky	No	No
15	8^0C	Reddish, little sticky	No	No
	Room temp.	Reddish	No	No
	40^0C	Reddish, sticky	No	No
30	8^0C	Reddish, little sticky	No	No
	Room temp.	Reddish	No	No
	40^0C	Reddish	No	No

Table No. 13: Observation of stability study

DAYS	TEMPERATURES		
	8^0C	**ROOM TEMP**	**40^0C**
8			

15			
30			

V. CONCLUSION:

From the present study, it is concluded that Salbutamol Sulphate Lollipops F3 formulation shows better looking Properties medicated lollipop. Hence it may be considered as perfect Formulation. sucrose based medicated lollipop may be a ideal dosage forms for pediatric patients for effective management of pharyngitis, tonsils, swollen gum. The stability studies proved that the prepared medicated lollipops were found to be stable when stored in air tight container over the storage period and at different conditions tested. These findings could be of potential use in designing such formulations for pediatric patient.

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