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Research Article of Formulation and Evaluation of Lozenges for Oral Bacterial Infection

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ABSTRACT

In present research work is the formulation and Evaluation of Roxithromycin lozenges for oral bacterial infection. In this current study, Roxithromycin macrolide category wide spectrum antibacterial drug was selected as a drug because the existing market product of Roxithromycin is not available in the form of lozenges that can deliver the drug from the oral cavity. In the present investigation, taste is one of the most important parameters of oral formulations so β-Cyclodextrin is used as a good taste masking agent for bitter drug and also enhance the solubility of the drug. Roxithromycin Compressed tablet lozenges were formulated by wet granulation technique with excipients like sucrose, lactose, citric acid, flavor and color and evaluated for organoleptic properties the test like diameter, thickness, weight variation, hardness, friability, mouth dissolving time, and % drug content. The Optimized formulation of Roxithromycin Compressed tablet lozenges (C_6) were sweet in taste, smooth in texture and having a diameter 13.708 ± 0.00 mm , thickness 6.704 ± 0.00 mm, hardness is 12 ± 1kg/cm^2 and drug content uniformity is 96 ± 0.02%. The weight variation and friability of lozenges (C_6) was passed as per IP and mouth dissolving time is found at 25 ± 2 min. *In vitro* dissolution study for roxithromycin compressed tablet lozenge was performed in pH 6.8 phosphate buffer wherein 95 % of the drug was released within 30 min.

INTRODUCTION

Oral drug delivery is the most preferred and simplest means as the oral route provides a maximum active surface area of all drug delivery system for administration of various drugs. The oral route of drug administration has been widely used for both conventional as well as novel drug delivery. [1, 2]

The lozenges are solid medicated, flavored and sweetened base dosage forms intended to be sucked and hold in the mouth or pharynx to treat local irritation, mouth or pharynx infection. Lozenges are one of the very popular and better innovative dosage form and oral confectionary products. It is a potentially useful for means of administration drugs either locally or systematically through the oral cavity. The reasons for this preference because of the easy to administered for the geriatric and pediatric patient, and widespread acceptance by patients. The development of new drug delivery systems for existing drug with an improved efficacy, avoid first pass hepatic metabolism, no need of water intake, and increase bioavailability together with reduced dosing frequency to minimum side effects.[3, 4, 5, 6,7]

Oral infection is a common public health problem. They can affect the tongue dorsum, lateral sides of tongue, buccal epithelium, hard palate, soft palate, supragingival plaque of tooth surfaces, subgingival plaque. [8, 9]

The antimicrobial drug is used to treat the oral infection. Roxithromycin, macrolide category wide spectrum antibacterial drug that inhibits bacterial protein biosynthesis by binding reversibly to the subunit 50S of the bacterial ribosome, thereby inhibiting translocation of peptidyl-tRNA. This action is mainly bacteriostatic at low concentrations, but can also be bactericidal in high concentrations. Roxithromycin is very slightly soluble in water and bitter in taste so inclusion complexation techniques are used to reduce of unpleasant taste, improving patient compliance and better therapeutics efficacy. [10, 11, 12]

MATERIALS AND METHODS

MATERIALS

Roxithromycin was received as a gift sample from Century Pharmaceuticals Limited, Vadodara, India. Sucrose, dextrose, lactose, citric acid, talc, magnesium stearate menthol, peppermint, acacia, gelatin and β Cyclodextrin were of used as an analytical grade.

METHODOLOGY

Pre-formulation studies:

Standardization of Roxithromycin by UV–Vis Spectrophotometric:

Standard Calibration of Roxithromycin in 6.8 Phosphate buffer:

Accurately weighed 50mg of Roxithromycin was transferred in 50 ml of volumetric flask and then 2ml of methanol was added to dissolve the drug and volume was made up to the mark by 6.8 pH phosphate buffer to get the concentration of 1000µg/ml. The further dilution of 5, 10, 15, 20, and 25µg/ml were prepared from the stock solution and absorbance was taken at 219 nm. The UV spectrum of Roxithromycin is shown in fig.1.

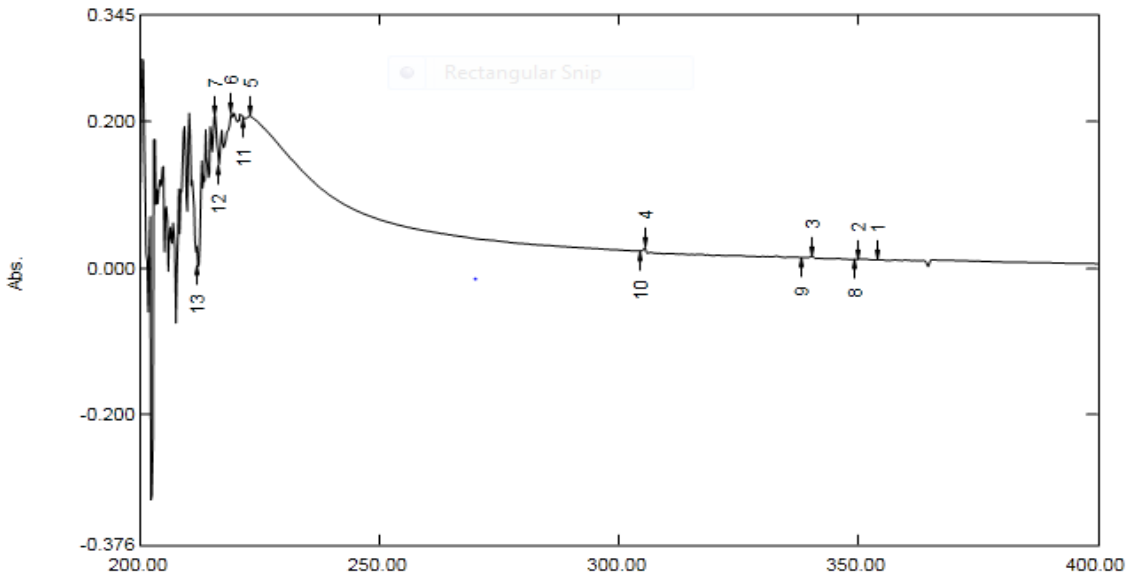

Fig.1: UV spectrum of Roxithromycin in Phosphate buffer in pH 6.8

Table 1: Optical characteristics of Roxithromycin

Parameters	Values
Absorption Maxima (nm)	219
Beer's range (µg/ml)	5-25 µg/ml
Regression equation (y)*	y = mx+c
Slope (m)	0.030
Intercept (c)	0.018
Correlation coefficient(R^2)	0.998

Table 2: Calibration Curve of Roxithromycin in Phosphate buffer in pH 6.8

Concentration	Absorbance Mean ±S.D. (n=3)
0	0.000 ± 0.000
5	0.184 ± 0.002
10	0.329 ± 0.001
15	0.474 ± 0.004
20	0.619 ± 0.001
25	0.764 ± 0.003

Fig. 2: Calibration Curve of Roxithromycin in Phosphate buffer in pH 6.8

Preparation of taste masking Roxithromycin by inclusion Complexation techniques:

By Solvent Evaporation Method:

In this method separately aqueous solution of β-CD (1:1) and an alcoholic solution of Roxithromycin were prepared then mixing of both solutions to get molecular dispersion of Roxithromycin and complexing agents and finally evaporating the solvent under vacuum to obtain solid powdered inclusion compound. The solid powdered was dried and pulverized and passed through mesh (#) 80 and stored in desiccators for further study.

Formulation of Compressed Tablet Lozenges:

Compressed tablet lozenges are usually harder than ordinary tablets so they will slowly dissolve in mouth. Tablet lozenges are usually based or vehicles which are sugar such as dextrose, sucrose and binders are also included to hold the particles of mass as discrete granules and include acacia, corn syrup, gelatin, polyvinylpyrrolidone, etc. These tablets differ from conventional tablets in terms of

- Organoleptic property,
- Non-disintegrating characteristics and
- Slower dissolution profiles.[5, 13]

Method of Preparation of Roxithromycin Compressed tablet lozenges:

Compressed tablet lozenges of Roxithromycin were prepared by wet granulation method. Firstly sugar was pulverized by mechanical comminuting to a fine powder and mixed with drug complex. Then acacia and gelatin mucilage, (color, flavor) were added to make dump mass. Then mass was subjected to granulation with sugar and screened through 22 mesh screen. Then granule were dried and passed through 44 mesh screen to form a uniform size of granules. Then granules were lubricated with magnesium stearate and talc. Then granules were compressed in a tablet using tablet machine. [5]

Table 3: Composition of Roxithromycin Compressed tablet lozenges

Ingredients	**C_1**	**C_2**	**C_3**	**C_4**	**C_5**	**C_6**
Roxithromycin	75 mg	75 mg	75 mg	75 mg	75 mg	75 mg
Sucrose	810 mg	810 mg	810 mg	810 mg	710 mg	710 mg
Dextrose	-	90 mg	-	-	-	-
Lactose	90 mg	-	90 mg	80 mg	160 mg	150 mg
Acacia mucilage	10 ml		5 ml	3 ml	3 ml	3 ml
Gelatin mucilage	-	10 ml		6 ml	6 ml	6 ml
Citric acid	-	-	5 mg	20 mg	30 mg	50 mg
Magnesium sterate	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Talc	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Coloring Agent	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Flavoring Agent	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg

Fig.3: Photograph of Optimized formulation

EVALUATION OF COMPRESSED TABLET LOZENGES OF ROXITHROMYCIN:

The prepared Lozenges were evaluated for following official and unofficial parameters like Organoleptic test, hardness, thickness, diameter, weight variation, friability, mouth dissolving time, drug content and *in vitro* dissolution studies etc.

❖ Organoleptic test:

Organoleptic properties were evaluated each batch of formulation manually. Organoleptic properties were an important parameter to be evaluated as change in Organoleptic properties like discoloration or surface roughness is an indication of instability of formulations. The Organoleptic test of prepared compressed tablet lozenges mentioned in below table 6.

❖ Diameter and Thickness:

The diameter and thickness were measured by using Vernier caliper. The tablet's dimensions are a very important factor in their manufacture. The three tablets were selected randomly from each batch of the formulation, and then thickness and diameter were measured. The average diameter and thickness for lozenges were calculated and observation reading mentioned in below table 7.

❖ Hardness:

The hardness of each batch formulation ten tablets was determined by using Monsanto Hardness tester. Mean and standard deviation were computed and reported. It is expressed in kg/cm^2. The average hardness for lozenges is calculated and presented with standard deviation and observation reading mentioned in below table 7.

❖ Weight Variation Test:

Twenty lozenges from the each batch formulation were randomly selected and weighed together the tablets were then weighed individually. The batch passes the test for weight variation test if not more than two of the individual lozenge weight deviates from the average weight by more than the percentage according to IP limits shown in table 4.

Table 4: Weight variation limit according to IP

Average Weight of Tablet (Mg)	% Deviation
Less than 80	10
80-250	7.5
More than 250	5

❖ **Friability:**

Friability was determined by using a Roche friabilator. Each batch formulation ten lozenges were weighed and placed in the Roche friabilator and all the parameters set on the friabilator. The apparatus was rotated at 25 rpm (100 rotations) for 4 minutes. After revolutions the tablets were deducted and weighed again. The maximum mean weight loss samples are not more than 1.0 %. The percentage friability was measured using the formula:

$$\%F = \frac{W}{} \times 100$$

and observation reading mentioned in below table.

Where, % F = friability in percentage,

W_0 = initial weight of lozenges

W = final weight of lozenges after revolution

❖ **Mouth Dissolving Time:**

Mouth Dissolving Time was determined by each batch formulation using USP disintegration apparatus, where lozenges were placed in each tube of the apparatus and time taken for the lozenges to dissolve completely was noted by using 900ml phosphate buffer of pH 6.8 at 37 ^{0}c. This test was done in triplicate. The average dissolving time for lozenges was calculated and presented with standard deviation.

❖ **Drug Content:**

Lozenges were powdered and dissolved in small volume of methanol in 50 ml volumetric flask and volume make up to 50 ml of Phosphate buffer at pH 6.8. From this solution 1 ml taken and

diluted with Phosphate buffer at pH 6.8 in 50 ml volumetric flasks then sonicated for 30 min then filtered using filter paper. The absorbance of this solution was measured at 219 nm using appropriate blank. The drug content of Roxithromycin lozenges was calculated using calibration curve and observation reading mentioned in below table 7.

RESULTS AND DISCUSSION

❖ *In Vitro* Dissolution Study:

A dissolution study was carried out in 900 ml of the dissolution medium (Phosphate buffer of pH 6.8) was placed in the vessels of the dissolution apparatus USP (type II). The dissolution medium was equilibrated to 37 ± 0.5 °C, and the paddle speed set to 50 revolutions per minute. Lozenges were placed in each of the vessels of the dissolution apparatus and operated at the specified rate. At specified time intervals of 5, 10, 15, 20, 25 and 30 min 5 ml samples were withdrawn from dissolution medium and 5 ml of fresh dissolution medium was added to the beaker. The vessel was kept covered for the duration of the test and the temperature of the medium maintained at 37 ± 0.5 °C at all times. The withdrawn samples were filtered and diluted up to 10ml phosphate buffer of pH 6.8 in a volumetric flask. The diluted filtrates were analyzed by UV spectrophotometer at a wavelength of 219 nm using a phosphate buffer of pH 6.8 as blank solution. Using the equation obtained from the calibration curve, the concentration of Roxithromycin in samples taken at time, 5, 10, 15, 20, 25, and 30 min were calculated the percentage drug release. A plot of percentage drug release against time was established.

Dissolution Conditions:

- **Dissolution Apparatus:** USP type II (Paddle)
- **Model:** Model-TDT 6P, Electro lab, Mumbai
- **Stirrer:** Paddle type.
- **Dissolution media quantity:** 900 ml
- **Dissolution media:** pH 6.8 (Phosphate buffer)
- **Temperature:** 37 ± 0.5^{o}C
- **Paddle RPM:** 50
- **Sampling intervals:** 5, 10, 15, 20, 25 and 30 min.

Table 5: Dissolution profile of Roxithromycin compressed lozenges C_6 batch

S. No.	Time (min)	Cumulative percent drug dissolved (n=3)			
		Set 1	Set 2	Set 3	(Mean ± SD)
1	5	49.23	50.13	49.03	49.46 ± 0.068
2	10	64.95	64.55	65.85	65.17 ± 0.067
3	15	71.17	72.43	71.76	71.78 ± 0.060
4	20	84.81	85.81	84.11	83.91 ± 0.133
5	25	93.51	92.51	93.81	93.27 ± 0.057
6	30	95.58	94.68	95.09	95.08 ± 0.0379

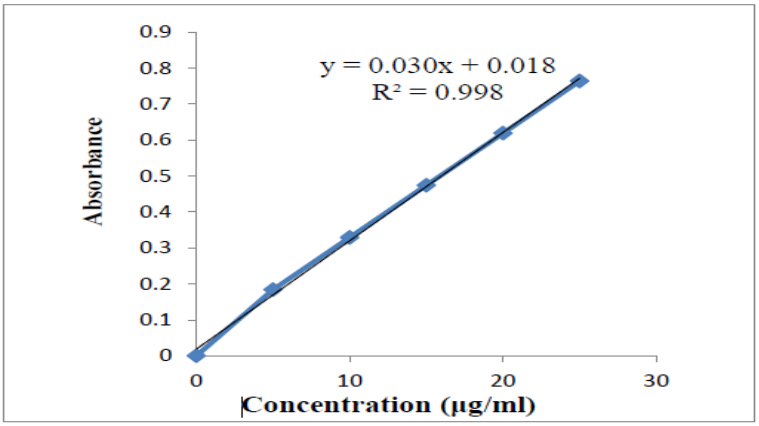

Fig.4: Dissolution profile of Roxithromycin in pH 6.8 Phosphate Buffer

From table 5 and figure 4of *In vitro* dissolution for lozenge was found that in pH 6.8 phosphate buffer 95 % drug was released within 30 min.

Table 6: Organoleptic examination of prepared compressed tablet lozenges

Parameters	Result
Shape	Spherical
Color	Light Pink
Texture	Smooth
Taste	Sweet

Table 7: Observation Reading of prepared compressed tablet lozenges

Formulation	Diameter	Thickness	Hardness	Weight Variation	Friability	Mouth dissolving time	% Drug Content
C_1	13.708 ± 0.00 mm	6.704 ± 0.00 mm	21 ± 1 kg/cm^2	Pass	Pass	22 ± 2 min.	91 ± 0.20
C_2	13.708 ± 0.00 mm	6.704 ± 0.00 mm	19 ± 1 kg/cm^2	Pass	Pass	25 ± 3 min.	94 ± 0.020
C_3	13.708 ± 0.00 mm	6.704 ± 0.00 mm	5 ± 1 kg/cm^2	Pass	Pass	24 ± 2 min.	95 ± 0.010
C_4	13.708 ± 0.00 mm	6.704 ± 0.00 mm	10 ± 1 kg/cm^2	Pass	Pass	25 ± 2 min.	94 ± 0.020
C_5	13.708 ± 0.00 mm	6.704 ± 0.00 mm	10 ± 1 kg/cm^2	Pass	Pass	25 ± 2 min.	92 ± 0.60
C_6	13.708 ± 0.00 mm	6.704 ± 0.00 mm	12 ± 1 kg/cm^2	Pass	Pass	25 ± 2 min.	96 ± 0.020

CONCLUSION

In present research work is the formulation and Evaluation of Roxithromycin compressed tablet lozenges for oral bacterial infection can be successfully developed with Roxithromycin complex of β Cyclodextrin is good taste masking and also enhance the solubility of drug.

It can be concluded that developed lozenge formulation prove to be were beneficial for local infection. Due to easy administrations and also improve the patient compliance. The lozenge onset of action could also be increased. The developed formulation can be used for treatment of local infection especially in case of pediatrics and geriatrics patients and those who can't swallow the drug.

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