IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Formulation And Evaluation Of Tinidazole Hard Candy Lozenges

[1]Teja Sri Soumya Kari, [2] Shanthi lysetty

[1]Assistant Professor, [2] Assistant Professor

[1]Pharmaceutics Department, Bharat Institute of Technology

[2] Pharmaceutics Department, Bharat Institute of Technology

Abstract: This study has been undertaken to develop hard candy lozenge formulation of Tinidazole which is an anti-protozoal,

Anti- bacterial agent, with sugar substitutes for effective management of trichomonasis, giardiasis and amoebiasis, this formulations helps to overcome the disadvantage of Tinidazole such as poor flow properties, bitter taste, abdominal pain etc. These Sugar free lozenges do not stimulate insulin and helps in reducing the risk factor for diabetics and also promote tooth cavities for young children. The method used is heating and congealing where isomalt is used as a low caloric sugar substitute. Optimized formulation **F4** with 0.01% plasticizer concentration was evaluated for various quality control parameters. Stability studies were conducted as per ICH guidelines. Hard candy lozenges were better formulations than marketed tablets with 98% release within 30 minutes. Low plasticizer concentration resulted in harder lozenges with minimum amount of processing problems.

Index Terms – lozenges, Hard candies, Isomalt, Heating and congealing .

I. INTRODUCTION

Buccal drug delivery system is a most promising route of drug delivery due to its rich vasculature and several advantages when compared to oral administration such as surpassing first pass metabolism, avoidance of pre-systemic elimination, effective drug localization in affected areas etc. [6.1] Lozenges are flavored medicated dosage forms intended to be sucked and held in the mouth or pharynx. They may contain vitamins, antibiotics, antiseptics, local anesthetics, antihistamines, decongestants, corticosteroids, astringents, analgesics, aromatics, demulcents or combination of these ingredients [6.2]. Hard candy is a mixture of sugar and other carbohydrates that are kept in an amorphous or glassy condition. This form can be considered as solid syrup of sugars generally having from 0.5 to 1.5% moisture content. Out of all the types of lozenges hard candies are better known for their stability and oral retention time. Tinidazole is an antiprotozoal, antibacterial agent used to cure bacterial and helminthic infections such as amoebiasis, trichomonasis, giardiasis etc. Tinidazole, a 5-nitroimidazole derivative w/ antimicrobial actions similar to metronidazole, is active against both protozoa (e.g. Trichomonas vaginalis, Entamoeba histolytica and Giardia lamblia) and obligate anaerobic bacteria. It damages DNA strands or inhibits DNA synthesis in microorganism.

II. MATERIALS AND METHODS

2.1. **Materials Used** Tinidazole gift sample from Granules India Pvt. Ltd, Hyderabad, Methyl cellulose (OHO chemicals Pvt. Ltd), Isomalt (Galen IQ 800) (Triveni chemicals Pvt. Ltd) Glycerol (Qualigens fine chemicals Pvt. Ltd), Peppermint oil (Central Drug House Pvt. Ltd), Citric acid (Thermo Electron Pvt. Ltd), Amaranth (Thermo Electron Pvt. Ltd). These are the materials used for the preparation of Tinidazole hard candy lozenges.

2.2. **Method of Preparation of Hard Candy Lozenges The Heating and Congealing technique [6.4] :** The syrupy sugar base was prepared in a beaker by dissolving isomalt in a little amount of water and was kept for heating on the hot plate till the temperature reached 150°C,temperatures was checked throughout the process with the help of a candy thermometer. When the syrup became thick, beaker was removed from the hot plate and was let to cool till it reaches 80°C. After cooling slowly, the medicament, citric acid, polymer, color plasticizer and hydrocolloid were added with continuous stirring. Finally, peppermint oil was added at the congealing phase and the mixture was poured into pre-lubricated moulds. Moulds were kept aside for 10 min after cooling lozenges were removed from the mould and wrapped in an aluminium foil and stored in the desiccators.

Table 1 : Formulation Trials

S.NO	EXCIPIENT	F1	F2	F3	F4
1.	Tinidazole (mg)	500	500	500	500
2.	Isomalt (mg)	450	450	450	450
3.	Methyl Cellulose (mg)	50	50	50	50
4.	Glycerin (mg)	0.63	0.38	0.25	0.13
5.	Citric Acid (mg)	25	25	25	25
6.	Sunset yellow supra (mg)	0.1	0.1	0.1	0.1
TOTAL WEIGHT (gms)		1.03	1.03	1.0253	1.0250

III. Evaluation tests for Hard Candy lozenges [6.5]

3.1. **Average weight and weight variation test:** 20 lozenges were selected and weighed collectively and individually on an electronic balance. From the collective weight, average weight was calculated. Each lozenge weight was then compared with average weight to assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 5% for 2 g lozenge and none by more than double that percentage. Average weight = weight of 20 lozenges / 20 % Weight variation= Average weight of lozenges-weight of each lozenge x 100 Average weight of lozenges.

3.2. **Friability Test** The friability of the 20 lozenges from each batch was tested by a friabiliator. At a speed of 25 rpm for 4 min. The lozenges were then de-dusted, re-weighed and percentage weight loss was calculated by the equation. **% Friability= (initial Wt.-Wt. after friability) x 100/initial. Wt.**

3.3. **Hardness Test** To evaluate the diametrical crushing strength, 3 lozenges from each formulation were tested using monsanto hardness tester. The mean ± SD values were calculated.

3.4. **Oral Retention Time [6.5] :**Oral retention time was determined for each batch of formulation using USP disintegration apparatus, where lozenges were placed in each tube of the apparatus and time taken for the lozenges to retain or time taken to dissolve completely was noted by using 100 ml of simulated salivary fluid at 37 °C.

3.5. **Preparation of Simulated Salivary Fluid** Sodium chloride (0.9 g) was dissolved in 95 ml distilled water and the volume was made up to 100 ml with human saliva. This preparation makes provision for isotonicity of actual human saliva, as well as necessary presence of resident salivary enzymes which

may impact on lozenge activity in normal clinical use condition. The mixture was sterilized by autoclaving at 121 °C at 15 lb. pressure for 30 min.

3.6. **Drug Content** Lozenges were powdered and equivalent powder was dissolved in 100 ml of pH 6.8 Phosphate buffer. From this solution 1 ml taken filtered using filter paper. The absorbance was measured at 273 nm. The drug content of Guaifenesin lozenges was calculated using calibration curve.

3.7. **Moisture Content Analysis Loss on Drying Method:** The sample was weighed and crushed in a mortar. From this, one gram of the sample was weighed and placed in desiccators for 24 h. After 24 h the sample is weighed. The moisture content is determined by the subtracting the final weight from initial weight of lozenges.

3.8. **In Vitro Dissolution Studies** The rate of the drug absorption was determined by the rate of drug dissolution from the lozenges. Thus, the rate of dissolution and bioavailability may be directly related to the efficacy of the lozenge. The USP type II dissolution apparatus was used and the dissolution medium was pH 6.8 phosphate buffer, 900 ml was placed in the beaker containing the lozenges and stirred at 50 rpm. 5 ml aliquot samples were withdrawn at 5 min. interval and replaced immediately with an equal volume of fresh buffer. Each aliquot was diluted and they were analyzed at 273 nm, by UV Visible spectrophotometer.

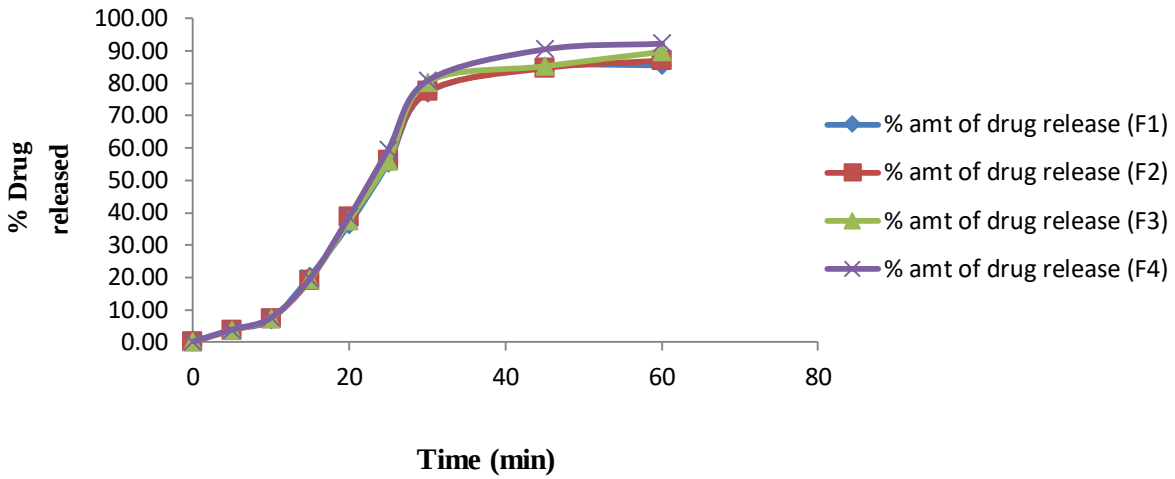

Fig 1 : Comparative in- vitro dissolution plots

3.9. **Stability Study** [6.6]: Accelerated stability study was carried out as per ICH guidelines Q1A (R2). The optimized formulation was wrapped in aluminium paper and was sealed. It was stored at accelerated (40°C±2°C/ 75% RH±5% RH) condition for a period three months. After every month lozenges were evaluated for drug content, weight variation, colour, hardness and moisture content.

3.10. **Comparison of Lozenges With Marketed Conventional Tablets** Optimized formulation was compared with normal marketed tablets of Tinidazole (Tinivista tablets manufactured by Forts India Laboratory).

Specifications of Tinidazole Tablet Name: Tinidazole tablet I.P
Strength: 500 mg **Brand name:** Tinivista **Company:** Cadila Pharmaceuticals Ltd
weight: 1000 mg

IV. RESULTS & DISCUSSION

4.1. **FT-IR Studies**: Infrared spectra for pure drug, Isomalt, and physical mixture were determined to find the compatibility of the drug in the mixture using FTIR-Spectrophotometer by KBr pellet method. The FTIR were performed and the spectra obtained are represented from **Fig 2 to Fig 4**, and no incompatibilities were found.

4.2.**Evaluation Tests for Hard Candy Lozenges[6.7]:**

The prepared hard candy formulations were tested with various evaluation procedures such as Organoleptic examination, hardness, weight variation, friability, thickness, moisture content, oral retention time, drug content, % in vitro drug release the results obtained were summarized in Table 2. All the formulations were meeting the requirements as per official **standards**. It was observed that all the lozenges with lower glycerol content had more hardness values which was a suitable result and the lozenges with higher methyl cellulose concentration showed more oral retention time that helps the lozenge to improve localized effect of drug and its bioavailability. The evaluation tests for optimized formulation F4 were summarized in Table 2 it showed a maximum hardness of 2 kg/cm^2 a better oral retention time of 25 min and a very minimum moisture content of 0.04% that was fulfilling stability criteria.

Table 2 : Evaluation tests of Optimised formulation F4

NAME OF THE TEST	F4 (OPTIMISED FORMULATION)
Weight variation test (± 5%)	0.29
Fraibility test (±1%)	0
Disintegration test (NMT 30 min)	10min
Thickness (NMT 5 cm)	3±
Hardness test (NMT 8 kg/cm2)	2±
Loss on drying (NMT 5%)	0.06
Dissolution (%)	92

4.3.**Stability Studies of lozenges:** For a period of three months the formulations were tested for all the evaluation parameters. The results for stability studies on hard candy lozenges were given in Table 3. There was not much significant difference in the lozenges parameters that were evaluated.

Table 3: Stability data

Evaluation parameters	0 day	After stability of 1 month	After stability of 2 month	After stability of 3 month
Organoleptic evaluation	No Change	No Change	No Change	No Change
Hardness	2±	5±	2±	2±
Weight variation	0.30	0.30	0.29	0.29
% Friability	0	0	0	0
Oral retention time	30	30	30	28
Drug content	98	98	97.5	97
Disintegration (min)	15	15	10	10
Moisture content	0.04	0.05	0.06	0.05

4.4.**Comparison with Marketed Formulation** The optimized formulations F4 was compared with the normal conventional commercial Tinidazole tablets for *in vitro* dissolution. The maximum drug release of marketed tablet was about 85.8% in 1 h this may be due to the higher amount of lubricants used during tableting process to overcome poor flow properties of Tinidazole . Whereas lozenges showed a better release of 92.26 % in a maximum of 60 min this is beneficial because we can localize the drug before its elimination.

V. CONCLUSION: Taste masking, stability enhancement and oral retention of drug are the current area of research. Increased drug retention increases the oral bioavailability and effective localization of drug was achieved in affected throat tissues. Gastro intestinal side effects of the drug can also be reduced. It was observed that the hard candies showed a better oral retention time, hardness and stability and drug release than and marketed tablet. Thus, by this work, we could conclude that lozenges can be used as efficient means of formulation to enhance palatability, oral retention and localization and avoiding tableting problems with drugs.

VI. ACKNOWLEDGEMENT

I sincerely acknowledge my Institution for providing me all facilities in fulfilling my research work.

VII. REFERENCES

6.1 Ramasamy N, Gopal V. 2014. Mucoadhesive Buccal Drug Delivery System-A Comprehensive And Promising Novel Drug Delivery. International Journal of Pharmaceutical Sciences and Research.; 5(4):1146.

6.2 Pothu R, Yamsani MR.2014. Lozenges formulation and evaluation: A review. IJAPR.; 1:290-4

6.3 Deng S, Huang W, Ni X, Zhang M, Lu H, Wang Z, Hu J, Zhu X, Qiu C, Shang D, Zhang Y. 2017 Oct 3.Pharmacokinetics of guaifenesin, pseudoephedrine and hydrocodone in a combination oral liquidformulation, administered as single and multiple doses in healthy Chinese volunteers, and comparison with data for individual compounds formulated as Antuss®. Xenobiotica.; 47(10):870-8.

6.4 McNally D, Simpson M, Morris C, Shephard A, Goulder M. 2010 Jan. Rapid relief of acute sore throat with AMC/DCBA throat lozenges: randomized controlled trial. International journal of clinical practice. 1;64(2):194-207

6.5 Nagoba SN, Rao KP, Sameer S, Gujrati DS, Nagoba BS. 2011. Studies on candy-based Ketoconazole Pediatric Tablet Lozenges. Int J Res Ayurveda Pharm.; 2(1):239- 43.

6.6 Esimone CO, Okoye FB, Odimegwu DC, Nworu CS, Oleghe PO, Ejogha PW. 2010.In vitro antimicrobial evaluation of lozenges containing extract of garlic and ginger. International Journal of Health Research.; 3(2):105-10.

6.7 Vidyadhara S, Sasidhar RL, Deepti B, Wilwin E, Sowjanyalakshmi B. 2015. Formulation and Evaluation of Amoxicillin Trihydrate Lozenges. Dhaka University Journal of Pharmaceutical Sciences.; 14(1):61-60