EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 11
Issue: 7
126-130
Year: 2024

FORMULATION AND EVALUATION OF ITRACONAZOLE MEDICATED CHEWING GUM FOR ORAL CANDIDIASIS

K. Ajith Kumar*, Dr. V. Kalvimoorthi, L. Gopi, Dr. K. Kaveri and D. Jeeva

Aadhibhagawan College of Pharmacy, Rantham, Thiruvannamalai, Tamil Nadu.

***Corresponding Author: K. Ajith Kumar**
Aadhibhagawan College of Pharmacy, Rantham, Thiruvannamalai, Tamil Nadu.

Article Received on 02/05/2024 **Article Revised on 21/05/2024** **Article Accepted on 12/06/2024**

ABSTRACT
Chewing gum is one of the most popular dosage form, used for delivering the many active components. Most of the chewing gums were used for smoking cessation (containing the nicotine) and also used for oral and dental hygiene. Itraconazole is an anti-fungal drug. It is one of the active ingredients used to treat oral candidiasis. In the present work medicated chewing gum of Itraconazole was developed to treat oral candidiasis. The study includes formulation and evaluation of medicated chewing gum of fluconazole. The chewing gum formulations were made using a gum base. The concentration of gum base was varied in the formulation to study its effect on in-vitro drug release. Formulations were developed by conventional/traditional method. The prepared formulations were evaluated for various parameters like physical appearance, weight variation, drug content in-vitro and in-vivo drug release behavior. Stability studies were conducted. From this study it could be concluded that it is possible to design medicated chewing gum containing Itraconazole, mainly for the treatment of oral candidiasis and related conditions.

KEYWORDS: Medicated chewing gum, Itraconazole, Oral candidiasis, Conventional/traditional method.

1. INTRODUCTION
Itraconazole, a synthetic antifungal agent of the imidazole class, is used to treat candidiasis. Thus it was attempted to design medicated chewing gum containing fluconazole, mainly for the treatment of oral candidiasis and related conditions where efficacy and enhanced patient compliance are of paramount importance. From the dissolution medium 5ml was withdrawn and volume made upto 10ml with SSF and the absorbance of the resulting solution was readed at 258nm.

2. DRUG PROFILE
2.1 ITRACONAZOLE
- **Boiling point:** 850 °C
- **Formula:** $C_{35}H_{38}Cl_2N_8O_4$
- **Molar mass:** 705.64 g/mol
- **Bioavailability:** 55%, maximal if taken with full meal
- **Protein binding:** 99.8%
- **Elimination half-life:** 21 hours
- **Excretion:** Kidney (35%), faeces (54%).

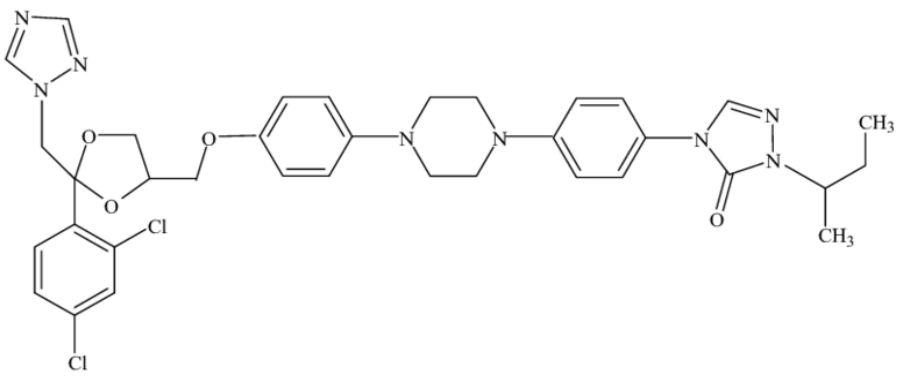

Fig: 1 Itraconazole Structure.

3. MATERIALS AND METHODS

3.1 METHODOLOGY

Gum base is softened by melting and placed in a mixer to which accurately weighed active ingredient (ITRACONAZOLE), bulk sweeteners (sucrose), and other excipients like sucrose, sorbital, talc, magnesium stearate, mint flavor and amaranth powder are added at a definite time. To melt all the ingredients and pour into mould. During this process a light coating of finely powdered sugar or sugar substitutes is added to keep the gum away from sticking and to enhance the flavor. in a carefully controlled room, the gum is cooled for up to 48hours. This allows the gum to set properly. Finally the gum is cut the desired size and cooled at a carefully controlled temperature and humidity.

Table No. 1: Formulation.

INGREDIENTS	F1	F2	F3	F4	F5	F6
ITRACONAZOLE	10	10	10	10	10	10
GAM BASE	100	100	100	100	100	100
SORBITAL	40	20	-	-	-	-
SUCROSE	100	120	-	120	-	-
CASTOR OIL	-	-	20	20	-	-
GLYCEROL	-	-	-	-	40	20
DEXTROSE	-	-	120	-	100	120
MG.STEARATE	15	15	15	15	15	15
MINT&AMARANT	15	15	15	15	15	15
TALC	20	20	20	20	20	20
TOTAL WEIGHT	300	300	300	300	300	300

4. EVALUATION

4.1 BULK DENSITY

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring pre sieved granules into a graduated cylinder via a large funnel and measure the volume and weight.

$$\text{Bulk density} = \frac{\text{weight of granules}}{\text{Bulk volume of granules}}$$

4.2 TAPPED DENSITY

Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the drug in the cylinder and this minimum volume, the taped density may be computed.

$$\text{Tapped density} = \frac{\text{weight of granules}}{\text{Tapped volume of granules}}$$

4.3 CARR'S INDEX (CI)

Carr's index is measured using the values of bulk density and tapped density. The following equation is used to find the Carr's index.

$$CI = \frac{(TD-BD)\ x100}{TD}$$

4.4 HAUSNER'S RATIO

It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or granules.

Hausner's Ratio = Tapped density/Bulk density

4.5 ANGLE OF REPOSE

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The method used to find the angle of repose is to pour the powder ion a conical heat on a level, flat surface and measure the included angle with the horizontal.

$$\text{Tan}\theta = h/r$$

4.6 PHYSICAL PARAMETER

The general appearance of a chewing gum including size, shape, colour, odour, taste having should be observed. It is must to have a good appearance for consumer acceptance. Physical changes may occur during storage, which can be determined PH and melting point using PH meter and melting point apparatus.

4.7 THICKNESS

The thickness and diameter of the formulated chewing gum were measured by using Vernier callipers.

4.8 WEIGHT VARIATION

The formulated chewing gum were tested for weight uniformity. 20 chewing gum were collectively and individually. From the collective weight, average weight was calculated. Each chewing gum weight was then compared with average weight to ascertain whether it is with in permissible limits or not.

4.9 HARDNESS

The chewing gum strength, which is the force required to break the chewing gum by compression in the diametric direction was measured in triplicate using Pfizer tablet hardness tester.

4.10 FRIABILITY

The friability of chewing gum will be determined by Roche Friabillator. 20 chewing gum were taken and weighed. After weighing the chewing gum were placed in the Roche Friabillator and subjected to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 RPM for minutes dropping the from a distance of six inches with each revolution. After operation the tablets were de-dusted and reweighed.

4.11 SENSORY EVALUATION

Sensory evaluation of chewing gum was done, following parameters were considered like color, taste, flavor, consistency and overall acceptability. On the basis of this evaluation following results came out.

4.12 INVITRO DISSOLUTION STUDIES OF ITRACONAZOLE CHEWING GUM

Table 2: Dissolution profile.

PARAMETER	DETAILS
Dissolution apparatus	USP – type II (paddle)
Medium	0.1N HCl
Volume	900ml
Speed	75rpm
Analytical method	UV - spectroscopy
λ max	258nm

5. RESULT AND DISCUSSION

5.1 CALIBRATION CURVE OF ITRACONAZOLE

The absorbance of the solution was measured at 258nm, using UV spectrometer with 1.2 PH gastric fluid as blank.

Table No: 3 Calibration Curve.

CONCENTRATION (µg/ml)	ABSORBANCE
2	0.1316
4	0.2419
6	0.3516
8	0.4615
10	0.5612

5.2 PRE COMPRESSION STUDIES

Table No. 4: Pre compression Studies.

CODE	BULK DENSITY (g/ml)	TAPPED BULK DENSITY	% COMPRESSIBILITY	HAUSNER'S RATIO	ANGLE OF REPOSE
F1	0.582±0.12	0.623±0.061	6.58±0.032	1.07±0.06	28°85'±0.025
F2	0.591±0.24	0.631±0.043	6.33±0.014	1.06±0.13	29°93'±0.041
F3	0.604±0.09	0.636±0.025	5.03±0.021	1.05±0.09	27°86'±0.068
F4	0.621±0.08	0.653±0.024	4.9±0.061	1.05±0.06	28°68'±0.054
F5	0.623±0.32	0.659±0.012	5.46±0.059	1.05±0.04	27°99'±0.043
F6	0.630±0.21	0.662±0.014	4.83±0.043	1.05±0.75	28°78'±0.015

5.3 PHYSICAL EVALUATION

Fig. 2: Itraconazole Chewing Gum.

After compression various quality control tests were carried out, following the organoleptic properties. Colour, odour, and shape.

Table No. 5: Physical Parameters.

Formulation	Colour	Appearance	Stickiness
F1	Pink colour	soft	Nil
F2	Pink colour	soft	Nil
F3	Pink colour	soft	Nil
F4	Pink colour	Hard	Nil
F5	Pink colour	soft	Nil
F6	Pink colour	soft	Nil

5.4 POST COMPRESSION STUDY

Table No: 6 Post Compression Study.

Code	Hardness	Thickness	Weight Variation	Friability	Drug Content
F1	3.45±0.24	3.58±0.12	300.2±0.21	0.16±0.015	95.12±0.22
F2	3.5±0.21	3.60±0.25	299.5±0.44	0.29±0.023	92.51±0.24
F3	3.6±0.30	3.59±0.20	299.6±0.31	0.13±0.016	93.55±0.24
F4	3.8±0.15	3.5±0.10	300.4±0.64	0.11±0.15	94.25±0.14
F5	4.0±0.13	3.58±0.06	301.6±0.14	0.24±0.098	91.38±0.12
F6	4.02±0.20	3.59±0.15	300.2±0.52	0.38±0.065	92.14±0.05

5.5 SENSORY EVALUATION

Table No: 7 Sensory Evaluation.

S.NO	PARAMETER	F1	F2	F3	F4	F5	F6
1	COLOR	9.5	9	9	9	9	10
2	TASTE	8.5	8.5	8.5	7.5	9.5	9
3	FLAVOUR	8	8	8	8.5	8.5	9
4	SHAPE	8	9	9	9	10	10
5	CONSISTENCY	8	8	9	9	9	9

1: extremely dislike, 2: strongly dislike, 3: moderate dislike, 4: slight dislike, 5:neutral, 6: slight like, 7: moderate like, 8: strongly like, 9: extremely like, 10: excellent

5.6 CUMULATIVE PERCENTAGE OF DRUG RELEASE PROFILE OF FORMULATION (F1 – F6)

Table No. 8: Drug Release.

TIME	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	26.12±0.15	29.37±0.76	32.23±0.16	36.12±0.62	38.79±0.75	41.74±0.32
10	37.21±0.09	42.15±0.94	46.12±0.28	49.51±0.15	53.24±0.19	57.28±0.16
15	45.67±0.08	51.16±0.15	56.20±0.12	60.23±0.42	65.18±0.37	69.43±0.43
20	58.23±0.03	62.18±0.19	67.23±0.89	69.12±0.98	70.28±0.75	79.39±0.75
25	65.12±0.48	71.15±0.23	76.13±0.91	78.35±0.32	81.76±0.54	87.95±0.82
30	73.34±0.89	80.38±0.32	85.12±0.32	87.19±0.28	92.15±0.27	97.62±0.19

6. CONCLUSION

Itraconazole is a anti fungal drug the drug selective inhibits the candidiasis lessons present in oral surface. The objects of present study was to investigate the possibility of chewing gum. The following conclusion can be drawn from the result obtained. The pre formulation studies like angle of repose, bulk density, tapped density, haunse radio and carrs index of all formulation were found to be within the standard limits. The chewing gum, were compressed and evaluated for post compression parameter like weight variation, thickness, hardness, friability, and drug content. All the formulation batches showed acceptable results. The in vitro drug release was studies with USP type-II dissolution apparatus in 0.1N Hcl for a periods of 24 hours. Results showed that formulations F6 shows better absorption 97.62% the drug release over a periods of 30 mins.

7. REFERENCES

1. Gadhavi AG, Patel BN, Patel DM, Patel CN. Medicated chewing gum, IJPSR, 2011; 2(8): 748-61.
2. Cloys L, Christen A, Christen J. The development and history of chewing gum, Bull Hist dent., 1992: 40: 57-65.
3. Malke SS, Shidhye SS, Desai AS, Kadam VJ. Medicated Chewing gum- A novel option, Indian drugs, 2006; 43(3): 191-98.
4. Surana AS. Chewing gum: a friendly oral mucosal drug delivery system, IJPSR, 2010; 4(2): 68-71.
5. Shirzad Azarmi, Wilson Roa, Raimar lobenberg. Current Perspectives in dissolution testing of

conventional and novel dosage forms, Int J pharm., 2007; 12-21.