

Formulation and Evaluation of Medicated Mouth Paint for Oral Thrush

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ABSTRACT: In the present work is aimed at oral retentive mouth paint preparations were designed and prepared for the effective treatment of oral candidiasis. Voriconazole, a triazole derivative having antifungal activity is chosen as model drug in this study. Voriconazole is used to treat oral candidiasis, which is a common infection in debilitated patients, AIDS patients and in persons who administer immunosuppressive drugs. Oral retentive mouth paints containing 1% Voriconazole with different hydrophilic polymers MC, HEC, NaCMC, PEG, glycerol, sodium citrate were formulated and evaluated for physical appearance, pH, drug content, rheological behaviour, spreadability, and FTIR spectral analysis. In vitro drug release studies were carried out at salivary pH 6.4 using cellophane membrane as barrier. Stability studies were carried out on all prepared formulations at ambient temp (RT), $30 \pm 1^\circ \text{C}$ at $65\% \pm 5\% \text{RH}$, $40 \pm 2^\circ \text{C}$ at $75\% \pm 5\% \text{RH}$ (accelerated temperature) for a span of 3 months and analyzed at different time intervals for drug content, physical appearance, pH, oral retention time and spreadability. All the prepared formulations were found to be stable.

KEY WORDS: Oral thrush, Voriconazole, drug release, Stability studies.

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I INTRODUCTION

Voriconazole is a triazole antifungal medication, it is generally used to treat serious, invasive fungal infections. These are generally seen in patients who are immunocompromised, and include invasive candidiasis, Oral thrush, invasive aspergillosis, and certain emerging fungal infections¹.

Oral thrush /candidiasis is a disorder caused by infection of the mouth due to fungus (yeast) candida albicans. Chronic thrush may develop, affecting the roof of the mouth in people who wear dentures. They are viscous preparations of medicaments for local action in the oral cavity. Glycerine as base is used because of its viscosity prevents it being washed away rapidly by saliva and thus a prolonged action may be obtained. They are applied in the mouth with a soft brush. The mouth paints are used in treatment of inflammation of various areas of the mouth and throat, which includes stomatitis, pharyngitis, laryngitis and tonsillitis. The common ingredients used in mouth and throat paint are anti infective agents like phenol iodine, gentian violet, boric acid and astringents like tannic acid for treatment of pharyngitis and tonsillitis. The Voriconazole mouth paints are flavoured medicated dosage forms intended to be sucked and hold in mouth and throat. The formulation is applied with brush in throat and patient is counselled for not to drink water immediately after application. The present investigation is designed to improve patient compliance. These preparations are commonly used for the purpose of local or systemic effects through the buccal mucosa. The present work is aimed at preparing a formulation of Voriconazole mouth paint which provide localized action and for protracted period of time to successfully treat oral candidiasis.

II OBJECTIVES:

The present work, it is planned to Formulate and Evaluate mucoadhesive mouth paints to treat oral candidiasis / thrush.

- Glycerin based formulation give soothing action in oral cavity with added advantage of sweetening agent with a flavour.
- MC, NaCMC, PEG, EC etc will be used as mucoadhesive polymers to enhance the transit time of formulation in oral cavity.
- Ease of administration, no skilled person is required for application. Brush is provided for applying the drug in mouth which prevents the contamination.

III MATERIALS AND METHODS

Voriconazole was received a gift sample from Glenmark Pvt. Ltd., Daman, Methyl cellulose (MC), ethyl cellulose (EC) and sodium CMC were obtained from Loba Chemicals Pvt. Ltd., Mumbai. Glycerine and PEG were obtained from SD fine Chemicals Pvt. Ltd., Mumbai. All other chemicals and solvents were of analytical reagent grade.

Preparation of medicated mouth paints

1. The preparation was carried out in varied batches following fusion and trituration technique.
2. Polymer, sodium citrate and glycerine were mixed together and kept for 24 hours for hydration.
3. Voriconazole was dissolved in 20 ml of propylene glycol and added to above hydrated base.
4. Then made up the volume with glycerol and mixture was stirred with three blade stirrer for 30 min at 50 rpm to get a homogenous dispersion of drug, Voriconazole 1% w/w.

Table: 1- Formulation of medicated mouth paints

Sl.No.	Ingredients	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
1.	Voriconazole	1 gm	1 gm	1 gm	1 gm	1 gm	1 gm
2.	MC	1.5 gm	-	-	2.0 gm	-	-
3.	EC	-	1.5 gm	-	-	2.0 gm	-
4.	NaCMC	-	-	1.5 gm	-	-	2.0 gm
5.	Sodium citrate	0.5gm	0.5gm	0.5gm	0.5gm	0.5gm	0.5gm
6.	Propylene glycol	20 ml	20 ml	20 ml	20 ml	20ml	20 ml
7.	Glycerol	q.s (100 ml)	q.s (100 ml)	q.s (100 ml)	q.s (100 ml)	q.s (100ml)	q.s (100 ml)

Physicochemical Characteristics of Formulated Voriconazole mouth paints^{9,10,11,12,13,14}

The prepared formulations were subjected to following parameters.

- a) Appearance b) Determination of pH c) Spreadability d) Viscosity e) Drug content

Drug-exceptient compatibility studies

The studies were carried out using FTIR method with the help of perkin-elmer 1615 spectrophotometer.

Stability Studies:

All the prepared formulations (F1, F2, F3, F4, F5 & F6) were subjected to stability studies at different temperature i.e., 30°C / 65% RH and 40°C /75% RH for a period of 3 months. There was no such considerable change in PH, Spreadability, Viscosity & drug content (no loss of drug more than 5%). In-vitro studies show no change in release.

In vitro drug diffusion studies:

In vitro drug diffusion study of voriconazole formulation, Phosphate buffer of pH 6.4 was used as the receptor fluid. Cellophane membrane was obtained from local market for this study. A glass cylinder with both ends open, 10 cm height, 3.7 cm outer diameter and 3.1cm inner diameter was used as permeation cell. A cellophane membrane (soaked in distilled water for 4 hrs before use) was fixed to one end of the cylinder with the aid of an adhesive to result in a permeation cell. 1 gm of prepared medicated mouth paint was taken in the cell (donor compartment) and the cell was immersed in beaker (150 ml) containing 100 ml of drug free phosphate buffer of pH 6.4 as receptor compartment. The cell was immersed to a depth of 1 cm below the surface of water in the receptor compartment. The medium in the receptor compartment was agitated using a magnetic stirrer and a temperature of 37⁰C ±1⁰C was maintained. Samples from receptor compartment (5 ml) withdrawn at the interval of 30 min over a period of 180 min and assayed for Voriconazole at λ_{max} 254 nm. The volume with drawn at each time (5 ml) was replaced with drug free receptor fluid (PBS of pH 6.4). All the studies were conducted in triplicate and S.D. was calculated.

Table-2 Physico-Chemical Parameters of Prepared Voriconazole mouth paint

Formulations	pH	Viscosity (cps)	Spreadability g.cm/s	Drug Content (%w/w)
F1	6.7	11700	11.23±0.68	96.11
F2	6.5	11980	10.76±0.76	96.89
F3	6.8	12220	11.13±0.51	97.49
F4	7.0	12575	12.06±0.53	98.05
F5	6.8	12710	12.95±0.60	98.95
F6	6.6	12877	9.86±0.80	97.78

Table: 3- In -vitro drug release of Voriconazole mouth paint

Time (Mins)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
30	11.94	12.76	12.90	13.94	15.66	13.10
60	21.58	22.80	23.79	24.58	28.88	23.85
90	32.09	33.83	34.66	35.09	43.93	35.76
120	41.89	42.77	44.88	47.89	59.57	45.98
150	50.49	53.89	56.78	58.49	73.89	56.98
180	62.67	64.66	67.65	69.67	89.88	70.15



Figure 1: oral thrush

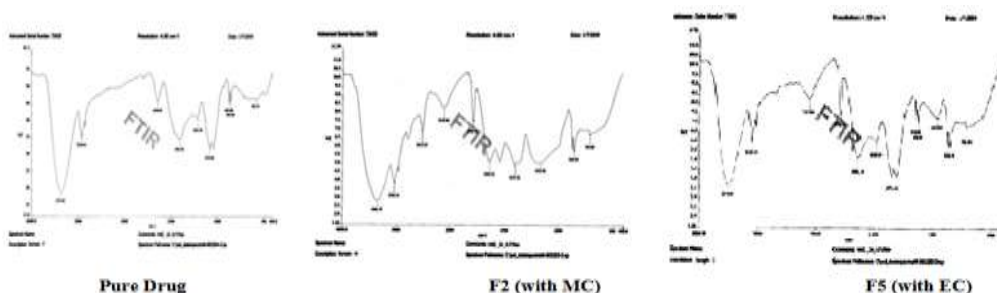
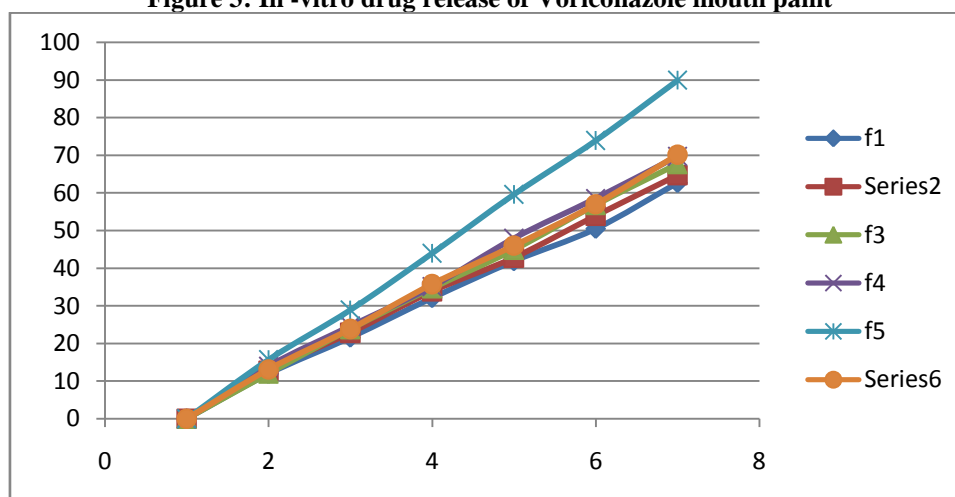


Figure 2: FTIR of Voriconazole mouth paint

Figure 3: In -vitro drug release of Voriconazole mouth paint



IV RESULT AND DISCUSSION

In the present study an attempt has been made to prepare medicated mouth paint using hydrophilic polymers MC, EC & NaCMC. Voriconazole is the drug of choice for the treatment of oral candidiasis due to its efficient antifungal action on causative organisms. Total six medicated mouth paints preparations of Voriconazole were prepared & evaluated for various parameters i.e.,

Determination of pH: pH of the prepared mouth paint was found to be 6.5 to 7.0 as shown in table-2.

Drug content uniformity: The percentage drug content of prepared mouth paint formulation was found to be 95 to 100% as shown in table-2.

Viscosity: The mean average viscosity was found to be 11700 to 12877 cps as shown in table-2.

Spreadability: The spreadability was found to be 9.86 ± 0.80 to 12.95 ± 0.60 g-cm/sec. as shown in table-2.

In-vitro drug release study: Results of in-vitro drug released from different formulations are shown in Table - 3 and graphically shown in Figure -3. The prepared formulations F5 shows better release profile as compare to other preparations i.e., F1, F2, F3, F4 & F6.

V CONCLUSION

Following conclusion can be drawn from the results obtained in the present work of investigation.

- The medicated mouth paint preparations of Voriconazole was prepared using hydrophilic polymers like MC, EC and NaCMC for the treatment of oral candidiasis.
- During our physicochemical evaluation studies all the formulations were found to have good spreadability and oral retention time.
- In our present investigation of in vitro diffusion studies, the formulation code F5 (containing 2.0% EC as base) showed optimum release 89.88 % in 3hrs.
- The formulation F₅ (containing 2.0% EC as base) showed good oral retention time 62 sec which measures the viscosity at physiological temperature.
- FTIR studies revealed that there is no drug excipients interaction.
- In our present investigation of stability studies, all prepared formulations did not segregate, ferment or physically deteriorated during storage and use at different temperature conditions for a period of 3 months. All the formulations did not undergo phase separation or gassing fermentation or otherwise deterioration aesthetically.
- The present study revealed that the prepared Voriconazole medicated mouth paint formulation with more retentive time in oral cavity will be useful than mouth rinses, gels and mouth paints which have short retentive time.

Hence the results of present study on medicated mouth paint designed for the treatment of oral candidiasis will be useful for drug industry to formulate localized drug delivery to benefit the patients suffering from oral candidiasis.

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