ORIGINAL ARTICLE

# Solubility of Drug Olopatadine Mouth Dissolving Film

**Ahirwar Varsha, Anjana Bharadwaj**

*Department of Pharmacy, Sarvepalli Radhakrishnan University, Bhopal, Madhya Pradesh, India*

## Abstract

**Objective:** This study was to perform their solubility of drug olopatadine oral film to evaluate their solubility mouth dissolving film in different solvent and artificial saliva and drug olopatadine hydrochloride solubility in different solvent. **Materials and Methods:** The olopatadine hydrochloride film was prepared by solvent casting method that is used for prepared oral strip solubility study in *ex vivo* method for avoid animal testing this study easy to help for solubility testing of film in saliva dissolution time solubility of drug to check in ultraviolet-spectrophotometric method. **Results:** The prepared oral strip showed satisfactory results for the evaluation parameters oral strip as optimized batch was evaluated. **Conclusion:** Overall this study indicated the enhancing the solubility of a poorly water soluble drug and this film formulation is easily solubilized the drug and its bioavailability is increased. Solubility of drug in different solvent is study in this formulation.

**Key words:** Artificial saliva, Film, Solubility, Solvent, Ultraviolet-spectrophotometric

## INTRODUCTION

Allergic is one of the most serious diseases and affects more than million people world-wide such as rashes, skin allergy, and pollution effective allergy grass allergy. This drug to prevent allergic reaction olopatadine drug is anti-histaminic H1 histaminic drug. Olopatadine is poorly dissolution this formulation of drug in mouth dissolving film, their solubility is good easy dissolve in saliva this study to enhanced their solubility for onset of action.[1] This solubility of drug in different solvent and formulation of film are dissolved in artificial saliva to check their solubility. This study was to perform easy to help their solubility study. Fast dissolving oral films are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improves the efficacy of active pharmaceutical ingredient's (APIs) by dissolving within minute in oral cavity after the contact with saliva without chewing or no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is 4–l000 time greater than that of skin.[2]

### Advantages of fast dissolving films

No special setup required for the industry availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity and promote the systemic absorption of APIs.. No need of water or a spoon for administration and without chewing. Dose accuracy in comparison to syrups.[3] Mouth dissolving film are directly dissolve in saliva and direct absorption to systemic circulation to act. Rapid onset of action. The drug enters the systemic circulation with reduced hepatic first pass effect.[3]

## MATERIALS AND METHODS

Olopatadine hydrochloride is a sample from drug from SRK University Bhopal (Sun pharmaceutical industries LTD.) Hydroxyl propyl methyl cellulose (HPMC-15) Oxford Laboratory, Mumbai, Maltodextrin (DE-20) Hamidia Laboratory Pvt. Ltd., Mumbai, Propylene glycol Loba Chemical Pvt. Ltd., Mumbai, Glycerin Sara fine chemical, Mumbai, Menthol Vikash pharma, Mumbai, Di sodium hydrogen phosphate Loba chemical Pvt. Ltd., Mumbai, Potassium dihydrogen phosphate Glaxosmith Kline pharmaceutical Ltd, Mumbai, Sodium chloride Loba chemical Pvt. Ltd., Mumbai, Ethanol Oxford Laboratory, Mumbai, and Methanol, Oxford Laboratory, Mumbai.

**Address for correspondence:**
Ahirwar Varsha, Sarvepalli Radhakrishnan University, Bhopal, Madhya Pradesh, India.
E-mail: varsha.ahirwar2010@gmail.com

**Received:** 27-03-2022
**Revised:** 18-05-2022
**Accepted:** 28-05-2022

### Preparation of oral stip

Film prepared by olopatadine hydrochloride by solvent casting method. Film was to evaluated different solvent for solubility. HPMCE-15 and Maltodextrin were dissolved in 10ml water kept aside for sometime and the solution was mixed with magnetic stirring machine [Figure 1] at 19–21 min. The solution was added propylene glycol and stirrer. The solution was kept aside for bubbles free solution sat overnight. This solution again stirring with magnetic stirrer at 60°c for 15 min and their solution was kept aside for few minutes for bubbles kept out. The mixture was kept aside for removal of air and then casted the mixture on petri dish and dried at hot air oven at 55°c for 31 min.[4] After dried, the film was prepared and cut 2 × 2 cm in size [Figure 2].

### For artificial saliva- composition of materials

For artificial saliva- composition of materials.

### Procedure of artificial saliva

Sodium chloride, potassium chloride, calcium chloride dehydrate, magnesium chloride hexahydrate, and potassium phosphate dibasic these ingredients were added one by one to 500 ml of distilled water and then the volume was made up to 1000 ml using the same. pH was adjusted with 0.1N hydrochloric acid to saliva pH 6.5–7.5.[5]

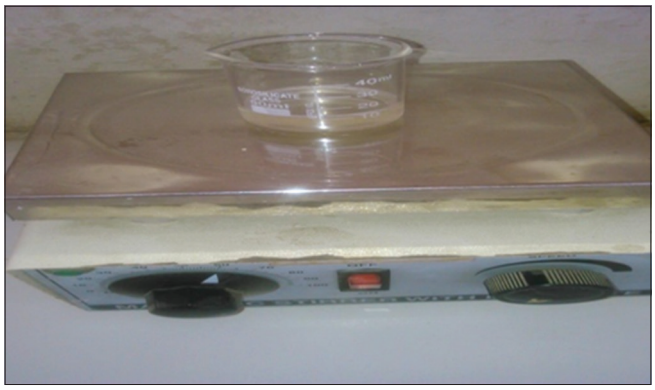


**Figure 1:** Magnetic stirring in magnetic machine

**Figure 2:** Fast dissolving oral film

### Evaluation of fast dissolving film

Film prepared by olopatadine hydrochloride by solvent casting method. Film was to evaluated different solvent for solubility.[6,7] The fast dissolving films of olopatadine HCL were evaluated for the following properties.

### Solubility of drug in different solvent

To evaluated the drug solubility in different solvent [Table 3].[8]

#### *Solubility*

1. One statement on solubility given under the heading solubility is not standards or test for purity but is provide primarily as information
2. A quantitative solubility test is given under "STANDARDS" the substance shall comply with this requirement
3. Statements of solubility are indicated by a descriptive phrase and are intended to apply at 20–30°.

The following table indicated the meanings of the terms used in the statement of approximate solubility.[5] [Table 4]

**1 FLOWCHART OF SOLUBILITY DRUG IN WATER**

Solubility of olopatadine HCL in water
0.01 g drug

↓

1 ml water→ solubility in 5 min→ not soluble

↓

10 ml water→ solubility in 5 min→ sparingly soluble

↓

20 ml water→ solubility in 5 min→ slightly soluble

↓

30 ml water→ solubility in 5 min→ soluble

Drug 0.01 g dissolve in 30 ml water continue stirring approximately 5 min, they are soluble in water.

## RESULTS AND DISCUSSION

### For artificial saliva- *ex-vivo* study

Part A – artificial saliva study – artificial saliva was prepared as per the method reported.[9] ingredients for artificial saliva [Table 2]. Artificial saliva test 5 ml of artificial saliva in a

**Table 1:** List of instrument and equipment

| Name | Manufacturers |
|---|---|
| Melting point apparatus | Jyoti scientific industries, Gwalior |
| Digital weighing balance | Jyoti scientific industries, Gwalior |
| UV spectrophotometer | PC-based double beam spectrophotometer 2202 systronic |
| pH meter | Advance scientific center, Bhopal |

**Table 2:** Ingredients for artificial saliva

| Ingredients | Quantity |
|---|---|
| Sodium Chloride | 0.844 g |
| Potassium Chloride | 1.2 g |
| Calcium Chloride Dehydrate | 0.193 g |
| Magnesium Chloride Hexahydrate | 0.111 g |
| Potassium Phosphate Dibasic | 0.342 g |

**Table 3:** Solubility of olopatadine HCL

| Solvent | Solubility of drug | Quantity of drug and solvent |
|---|---|---|
| Acetonitrile | soluble | Drug 0.01 g dissolve in 10 ml acetonitrile |
| Methanol | Freely soluble | Drug 0.01 g dissolve in 10 ml Methanol |
| Distilled water | Sparingly soluble | Drug 0.01 g dissolve in 10 ml Distilled water |
| Ethanol | Freely soluble | Drug 0.01 g dissolve in 10 ml Ethanol |

Petridis and dip the fast dissolving film in these saliva, in a few seconds, film was properly dissolved these artificial saliva [Graph 1].

### Solubility of drug in buffer solution

To evaluated the drug solubility in different solvent.[8]

### Solubility

1. One statement on solubility given under the heading solubility is not standards or test for purity but is provide primarily as information [10]

2. A quantitative solubility test is given under "STANDARDS" the substance shall comply with this requirement

3. Statements of solubility are indicated by a descriptive phrase and are intended to apply at 20–30°.

**Table 4:** Solubility of drug in water[12]

| Descriptive Term | Approximate volume of solvent in ml/gm. of solute, solubility of olopatadine HCL in water |
|---|---|
| Not soluble | <1 ml water/0.01 g drug |
| Sparingly soluble | 10 ml water/0.01 g drug |
| Slightly soluble | 20 ml water/0.01 g drug |
| Soluble | 30 ml water/0.01 g drug |

**Table 5:** For buffer solution

| Ingredients | Quantity |
|---|---|
| Disodium Hydrogen Phosphate (Oxford Laboratory) | 28.20 g |
| Potassium Phosphate Dibasic Anhydrous (Loba. Chemi. Mumbai) | 11.45 g |
| Water | Q.S |

**Table 6:** Preparation of standard solution for calibration graph

| Volume taken in Ml From Stock B | Conc. (µg/ml) |
|---|---|
| 0.5 | 2 |
| 1.0 | 4 |
| 1.5 | 6 |
| 2.0 | 8 |
| 2.5 | 10 |

The following table indicated the meanings of the terms used in the statement of approximate solubility.[5]

### For buffer solution PH 6.8

Dissolve 28.20 g of disodium hydrogen phosphate and 11.45 g of potassium phosphate dibasic anhydrous in sufficient water to produce 10000 ml [Table 5].

#### *Dissolution of drug in buffer solution*

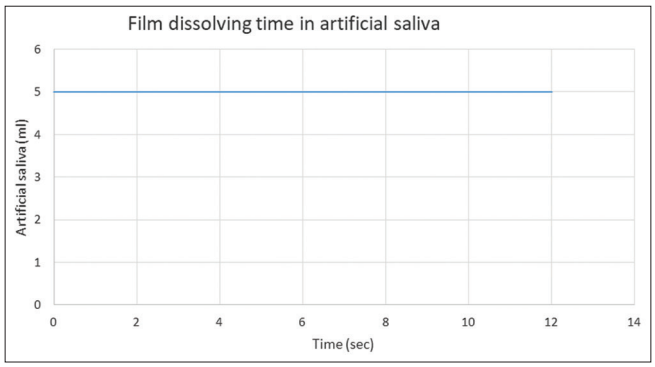
Dissolution of drug time-freely soluble in buffer solution time – 5.8 s. In the present work, a simple, selective, rapid, precise, and economical ultraviolet (UV) spectrophotometric method has been developed and validated for the estimation of the olopatadine HCL fast dissolving film dosage form.[9]

#### *Chemicals and solvents*

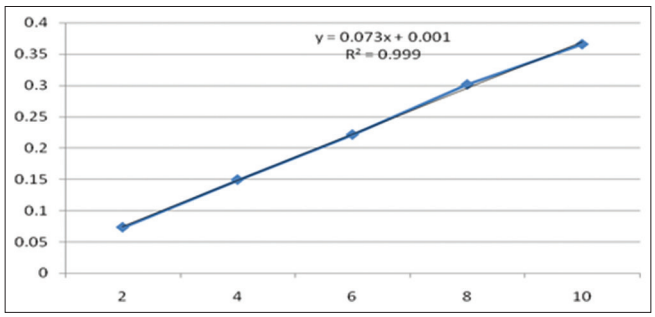
- Olopatadine Hcl- Sunpharma Pharmaceutical Ltd.
- Distilled water – Rankem
- Methanol-Fisher Scientific.

**Table 7:** Data for laboratory samples analysis

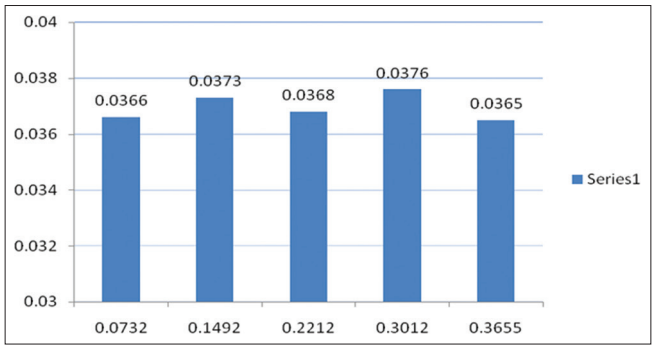
| Conc. of drug(µg/ml) | Replicate | Abs at 290.5 nm | Concentration Found | % Mean |
|---|---|---|---|---|
| 2 | I | 0.0732 | 1.99 | 98.1 |
| | Ii | 0.0739 | 1.98 | |
| | Iii | 0.0722 | 1.91 | |
| 6 | I | 0.2112 | 5.97 | 99.72 |
| | Ii | 0.2012 | 5.96 | |
| | Iii | 0.2410 | 6.01 | |
| 10 | I | 0.3655 | 9.89 | 98.83 |
| | ii | 0.3659 | 9.97 | |
| | iii | 0.3650 | 9.79 | |
| | | | Mean | 98.88 |
| | | | S.D. | ±0.8115 |




**Graph 1:** Calibration curve of film dissolve in artificial saliva contain conc. of drug




**Graph 2:** Calibration curve of olopatadine HCL




**Graph 3:** Response ratio curve of olopatadine HCL

### *Method development*

- Determination of solubility
- Selection of solvent system
- Study of spectra of drug and selection of suitable method
- Wavelength selection for linearity study
- Linearity range and calibration graph
- Film dissolved in saliva.

### *Solubility*

Solubility of drug was observed by dissolving in different solvents.

### *Selection of solvent system*

The solution of olopatadine HCL was prepared in various solvent systems and scanned over the UV range (200–400) in spectrum mode at slow scan speed, distilled water and methanol were selected as the best solvent system.[11]

The methanol is selected because-

a. Drug is soluble in it
b. Drug is stable in it
c. Drug shows good spectra in it.

### *Study of spectra and selection of suitable method*

From stock solution, concentration of 10 µg/ml for olopatadine HCL was prepared. Drug was scanned over the range of 200–400 nm, while studying the spectra, it was observed that olopatadine HCL shows maximum absorbance at 290.5 nm, drug can be estimated by simple direct measurement of absorbance at its $\lambda_{max}$.[12]

### *Selection of wavelength for linearity*

The wavelength was selected, to study the linearity of olopatadine HCL in the maximum absorbance maxima ($\lambda_{max}$), that is, max of Olopatadine Hcl: 290.5 nm.

### *Linearity and calibration graph*

#### *Linearity range*

Different dilutions of olopatadine Hcl between 0 and 100 µg/ml were scanned at their λmax in UV range and found that olopatadine Hcl follows linearity between 2 and 10 µg/ml.[13]

#### *Calibration Graph*

Accurately weighed 50 mg olopatadine Hcl was transferred into 50 ml volumetric flask and dissolved in methanol, then volume was made up to 50 ml with distilled water to get a concentration of 1000 µg/ml (Stock-A). 2.5 ml of Stock-A of olopatadine Hcl was taken in 25 ml volumetric and diluted up to 25 ml to get concentration of 100 µg/ml (Stock-B). Finally, from stock Solution-B, different of 2, 4, 6, 8, and 10 µg/ml were prepared for analysis. Absorbance was observed at 290.5 nm. Linearity was observed by the linear regression equation [Graph 2] and correlation coefficient was found to be 0.999 [Graph 3].[5]

### Preparation of standard solution for calibration graph

From the stock solutions, aliquots diluted up to 25 ml with distilled water to obtain the concentrations [Table 6].

### Standardization of the method

To confirm the validity of the method, laboratory samples containing olopatadine HCL were prepared, in the range of 2–10 µg/ml. The amount of drug present in the standard solution was calculated using the selected linearity equation and the results are tabulated in Table 7.[13]

## CONCLUSION

- In the present work, The olopatadine HCL is insoluble in water and its bioavailability is limited and, hence, this method is useful for improving its bioavailability of the drug. These formulations are avoid first pass metabolism and its very helpful for dysphagia patient. Short term stability studies of promising formulation indicated that there is no significant change in drug content and *in-vitro* dissolution time. This study was to enhance drug solubility in the formulation
- Dissolving film in different solvent and artificial saliva, solubility study was in *ex vivo* method for avoid animal testing, this study was easy to help for solubility testing of film in saliva dissolution time solubility of drug to check in UV-spectrophotometric method. Overall this study indicated the enhancing the solubility of a poorly water soluble drug and this film formulation is easily solubilized the drug.

## ACKNOWLEDGMENT

The authors wish to acknowledge the College Sarvepalli radhakrishnan university, Bhopal India, for providing the necessary facilities and support to carry out this project.

## REFRENCES

1. Bobade NN, Atram SC, Wankhade VP, Pande SD, Tapar KK. A review on buccal drug delivery system. Int J Pharm Pharm Sci Res 2013;3:35-40.
2. Abdelbary A, Bendas ER, Ramadan AA, Mostafa DA. Pharmaceutical and pharmacokinetic evaluation of a novel fast dissolving film formulation of flupentixol dihydrochloride. AAPS PharmSciTech 2014;15:1603-10.
3. Chaudhary H, Gauri S, Rathee P, *et al*. Development and optimization of fast dissolving orodispersible films of granisetron HCL. Bull Facult Pharm Cairo Univ 2013;51:193-201.
4. Chaudhary H, Gauri S, Rathee P, Kumar V. Development and optimization of fast dissolving oro-dispersible films of granisetron HCL using box behnken statistical design. Bull Facult Pharm Cairo Univ 2013;51:193-201.
5. As Per Indian Pharmacopeia (IP) Volume-1; 1996 Addendum 2000.
6. Bala R, Khanna S, Pawar P. Design optimization and *in vitro-in vivo* evaluation of orally dissolving strips of clobazam. J Drug Deliv 2014;2014:392783.
7. Daud A, Bonde M, Sapkal N, Bonde M. To study the effect of solvent, viscosity, and temperature on the mouth-dissolving film of *Withania somnifera* Linn. Asian J Pharm 2012;6:212-7.
8. Zhang H, Han M, Wang Y, Zhang J, Han ZM, Li SJ. Development of oral fast-disintegrating levothyroxine films for management of hypothyroidism in pediatrics. Trop J Pharm Res 2015;14:1755-62.
9. As Per Indian Pharmacopoeia (IP) Volume 2; 2007 Addendum 2008.
10. Zaidan M, Soufi L, Hafeez M, Abdelwahid M, Rasul KI. Assessing prescribing patterns for the prevention of chemotherapy induced nausea and vomiting in the national centre for cancer care and research. Saudi Pharm J 2015;23:381-7.
11. Yeh C. Hyperemesis gravidarum. J Chin Med Assoc 2017;J Chin Med Assoc:1-2.
12. Bhatt YJ. To develop simple and economical UV spectrophotometric method for the estimation of olopatadine and ketorolac tromethamine in ophthalmic dosage form, for the treatment of conjunctivitis. Int J Pharm Sci Rev Res 2013;20:118-20.
13. Fu Y, Yang S, Hoon JS, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, tastemasking and clinical studies. Crit Rev Ther Drug Carrier Syst 2004;21:433-75.

**Source of Support:** Nil. **Conflicts of Interest:** None declared.