Original Article

# Development And Characterization Of Orally Disintegrating Film Of Dextromethorphan For Improved Patient Compliance

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**DOI:** 10.47750/pnr.2022.13.S10.1313

## Abstract

Fast-dissolving pills are becoming more and more common because they don't need water to be administered. Dextromethorphan is prescribed for sore throats. The study's goal was to develop and improve a fast-dissolving film for dextromethorphan taste masking utilizing a casting approach using HPMC E15 LV, polyethylene glycol 400, aspartame-tartaric acid- citric acid- menthol-ion exchange resins. Plasticizers, tartaric and citric acids, which stimulate salivation, menthol, and tartaric and citric acids as flavouring agents were all used in the formulation of the films. To disguise the bitterness of medications, Aspartame and Kyron T111, an ion exchange resin, were employed as sweeteners. According to a study on drug content in films that dissolve quickly, more than 95% of the medications are present. More than 96% of pharmaceuticals are released within 30 minutes, according to a formula film that demonstrated a 17-second oral dissolving time. Without using any organic solvent, films were made using the solvent casting process, and it was discovered that they satisfied the mouth dissolving time and other film criteria. Our findings indicate that the four films we developed all had satisfactory film characteristics. Conclusion: Without using any organic solvents, a fast-dissolving film containing dextromethorphan may be cast using the solvent casting process.

**KEYWORDS:** Dextromethorphan; HPMC E15LV; PEG 400; Kyron T111

## Introduction

Among all the ways that have been investigated for systemic drug delivery via diverse products of varied dosage forms, oral drug delivery has been recognized for decades as the most frequently used route of administration. The fact that the oral route is so widely used may be due in part to its simplicity of administration as well as a long-held notion that drugs taken orally are just as well absorbed as foods consumed on a daily basis. Up to 50–60% of all dose forms are administered by the oral route, which has gained widespread approval. Solid dose forms are preferred because they are simple to administer, precise in their amount, allow for self-medication, reduce pain, and, most significantly, increase patient compliance. oral application for When mixed with saliva, fast disintegrating/dissolving tablets (FDT) like these quickly disperse to create a suspension or solution of the medicine that patients can easily swallow.

Most of the time, a fast-dissolving film is one that dissolves or disintegrates in the mouth without the use of water or chewing. The active components in the majority of quick dissolving delivery system films must be taste-masked by other compounds. The patient's saliva then swallows this concealed active ingredient along with

the soluble and insoluble excipients. The target demographic for these new fast-dissolving dose forms has typically been children, the elderly, and patients who are bedridden or physically disabled. Fast-dissolving tablets are also a useful option for patients with persistent nausea, those who are travelling, or those with little or no access to water. Another factor contributing to the rise in quickly dissolving/disintegrating products is pharmaceutical marketing. Fast dissolving film combines the benefits of traditional tablet and liquid formulation, providing advantages over both conventional dosage forms (Saini et al. 2011, Nagar et al. 2011). This is its main advantage. A very thin oral strip serving as the delivery mechanism is simply placed on the patient's tongue or any other oral mucosal tissue. Upon being instantaneously moistened by saliva, the film quickly hydrates and binds to the application site. When eaten, it quickly decomposes and dissolves, releasing the drug for oromucosal absorption or, with formula adjustments, maintaining the quick-dissolving characteristics to enable gastrointestinal absorption. The quick films can be created using a manufacturing procedure that is competitive with the manufacturing costs of regular tablets, in contrast to other existing rapid dissolving dosage forms, which are composed of liophylisates. In 2010 (Arya et al.)

The study's goal was to develop and improve a fast-dissolving film for dextromethorphan taste masking utilizing a casting method using HPMC E15 LV, polyethylene glycol 400, aspartame, citric acid, menthol, and ion exchange resins.

## Materials and Methods

Drugs (Dextromethorphan,) Polymers (HPMC E15 LV, HPMC E5 LV, PVA Plasticizers PEG 400), Super disintegrants (Cross Carmellose Sodium), Sweeteners-(Aspartame, Neotame, Sucralose, Sodium saccharin, Liquorise), Flavors (Menthol), Ion Exchange resin (Kyron T111), Food Color FDA approved orange color. Dextromethorphan was obtained from Vivian laboratories, kalol, as gift samples. All other excipients were of laboratory grade from ACS laboratories Ahmedabad.

## Formulation of Fast Dissolving Film

In general, rolling, semisolid casting, solvent casting, hot melt extrusion, and solid dispersion extrusion are used to create the mouth-dissolving film. Solvent casting without the use of organic solvents is currently the favoured manufacturing method for this film. Heat was used to dissolve the polymer (HPMC E5 LV, HPMC E15 LV, and PVA) in 5 ml of water. In order to prevent air entrapment, plasticizer (PEG 400) and super disintegrants (Cross Carmellose sodium) were added to the polymeric solution. The solution was then set aside for two hours. Three millilitres of water were used to dissolve the medications (Dextromethorphan) and sweetners (aspartame, neotame, perlitol, sucralose, liquorice, and saccharin sodium). To create a homogenous, viscous solution, drug solutions were added to the polymeric solution and agitated for one hour. The viscous solution, which had no bubbles, was cast into a casting plate with a diameter of 50.24 $cm^2$. The film is then allowed to dry on the casting plate for 12 hours at room temperature. The dried film was then shaped and measured into 2 $cm^2$ pieces for the desired use.

## Evaluation of Fast Dissolving Film

### FTIR spectroscopy

The medicine Dextromethorphan and the excipients HPMC E15 LV were tested for compatibility using a Fourier Transformed Infrared (FT-IR) spectrophotometer to rule out any potential chemical reactions. It was done using the potassium bromide pellet method for infrared spectroscopy. In a spectrophotometer, the particle was scanned from 4000-400 cm-1. Shimadzu Co., Kyoto, Japan; FTIR-8300).

### Weight variation of film

Two square inch film was cut at five different places in the cast film. The weight of each film/ strip was taken

and the weight variation was calculated. (Bodmeier et al., 1990)

## Thickness of film

The thickness of film was performed by screw gauge at different position of the film and the average thickness was calculated. (Patro et al., 2011, Hasan et al., 2012)

## Folding endurance

The folding endurance is expressed as the number of folds (number of times of film is folded at the same plain) required breaking the specimen or developing visible cracks. This gives an indication of brittleness of the film. A small strip of 2 cm2 was subjected to this test by folding the film at the same plane repeatedly several times until a visible crack was observed. (Hasan et al., 2012, Malladi et al., 2011, Subramanian et al., 2010)

## Disintegration time

Disintegration time was performed using disintegration test apparatus. Two square inch film was placed in the basket, raised and lowered it in such a manner that the up and down movement was done at a rate equivalent to thirty times a minute. Time required by the film, when no traces of film remain above the gauze was noted. (Mishra et al., 2011, Kalyan et al., 2012)

## Mouth dissolving time

The mouth dissolving time was determined by placing the film manually into a petridish containing 10 mL of 6.8 pH phosphate buffer. Time required by the film to dissolve was noted. (Kiran et al., 2011, Seth et al., 1997)

## % Drug content

The films were evaluated for % drug content. Films of size two square inches was cut, placed in 100 mL of volumetric flask and dissolved in phosphate buffer of pH 6.8, volume was made up to 100 mL. One ml of the solution from the 100 mL volumetric flask was taken into 10 mL of volumetric flask and made the volume up to 10 mL with methanol. The absorbance of the solution was measures at 227 nm for Dextromethorphan. (Patel et al., 2009)

## In vitro dissolution study

Dissolution study was carried out using USP type I (basket apparatus) with 300 mL of 6.8 pH phosphate buffer as dissolution medium maintained at 37 ± 0.5 oC. Medium was stirred at 50 rpm for periods of 30 min. Samples were withdrawn at 2, 5, 10, 15, 20 and 30 min interval, replacing the same amount with the fresh medium. From withdrawn samples 1 mL of solution was taken and was diluted up to 10 mL with methanol and analyzed at 220.5 and 227.5 nm wavelengths for Cetirizine and Dextromethorphan respectively. (Borsadia et al., 2005, Patel et al., 2009)

## Accelerated stability study

The stability study is performed to check physical and chemical integrity of the formulation. The selected batches were subjected for stability study. All the FDF were suitably packed in aluminum foil. The FDF to be tested at room conditions were kept outside in a petridish. At the end of every week the sealed FDF were opened and evaluated for different parameters.

# Results and Discussion

## FTIR spectroscopy

The individual drugs and both the combination of drugs and drugs with polymer were separately scanned. All

the spectra were compared for confirmation of common peaks. Dextromethorphan and combination with polymer showed no significant variation in intensity and position peaks, suggesting that drugs and excipients were compatible. Hence, it can be concluded that the drug Dextromethorphan is in Free State. The spectra are reported in the figures- 1, 2. The individual IR spectrum of the pure drugs was also found to be similar to that of its standard spectrum.

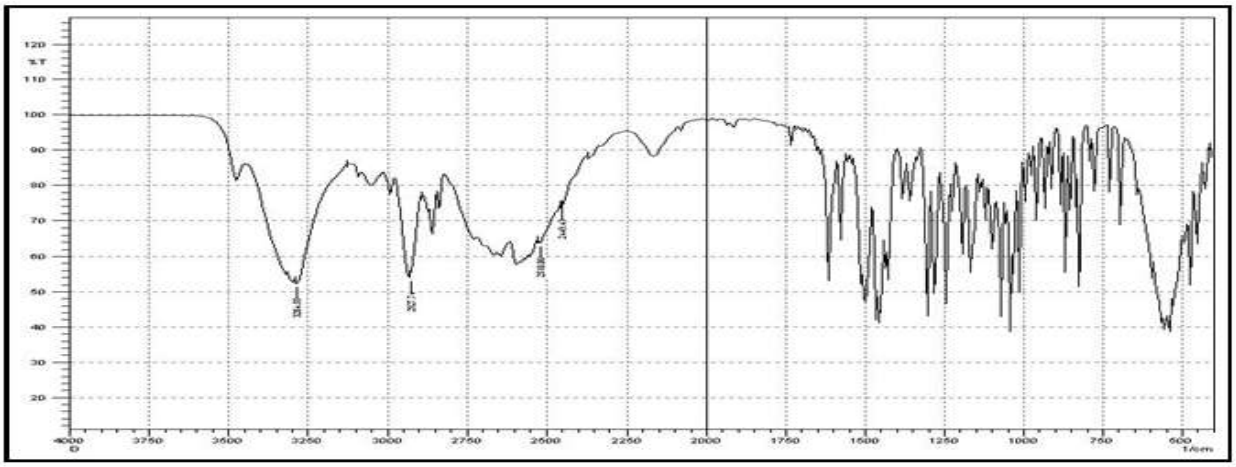

**Figure 1.** FTIR spectra of Dextromethorphan.

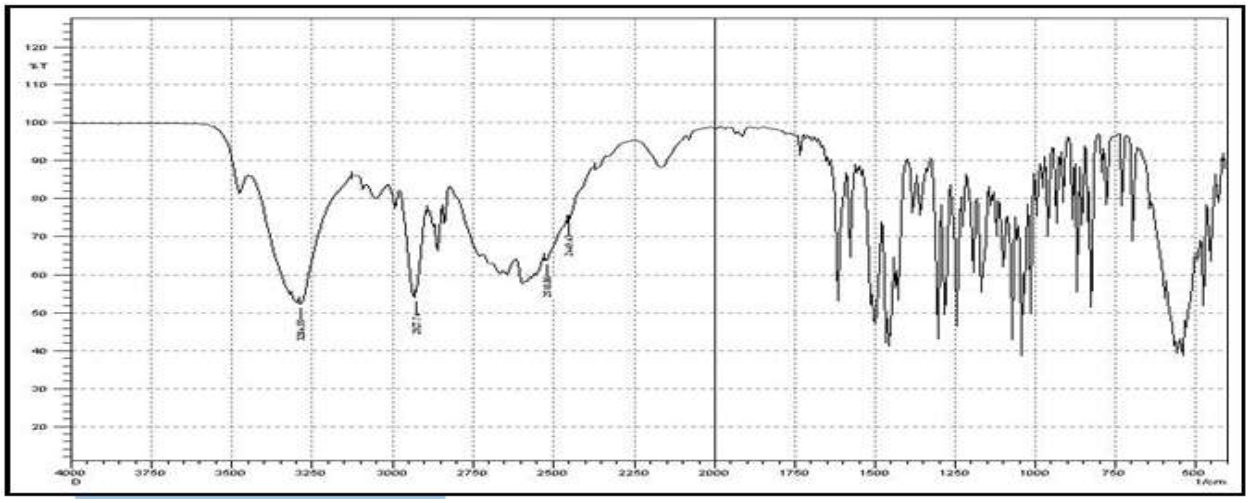

**Figure 2.** FTIR spectra of Dextromethorphan with HPMCE15LV

## Formulation of Fast Dissolving Film

Among all the different polymers, HPMC E15 LV polymer containing film was found to have good appearance with less thickness as much as 2 mm and less mouth dissolving time of 28 sec. The film containing PVA was difficult to remove from casting plate and with HPMC E5 LV there was increase in mouth dissolving time up to 32 sec. therefore HPMC E5LV and PVA were not used for further relevant process.

**Table 1. Screening of polymers for fast dissolving film.**

| S. No. | Ingredients | P1 | P2 | P3 |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| 1 | Dextromethorphan | 125.6 | 125.6 | 125.6 |
| 2 | HPMC E5 LV | 800 | - | - |
| 3 | HPMC E15 LV | - | 800 | - |
| 4 | PVA | - | - | 800 |
| 5 | PEG 400 (mL) | 1 | 1 | 1 |
| 6 | Sachharin sodium | 220 | 220 | 220 |
| 7 | Cross carmelose sodium | 200 | 200 | 200 |
| 8 | Citric acid | 80 | 80 | 80 |
| 9 | Tartaric acid | 80 | 80 | 80 |
| 10 | Menthol | 0.02 | 0.02 | 0.02 |
| 11 | Water (mL) | 10 | 10 | 10 |

*(All the quantities are in mg)

**Table 2. Effect of amount of HPMC E15 LV on disintegration time of fast dissolving film.**

| S. No. | Ingredients | H1 | H2 | H3 | H4 | H5 | H6 | H7 |
|---|---|---|---|---|---|---|---|---|
| 1 | Dextromethorphan | 125.6 | 125.6 | 125.6 | 125.6 | 125.6 | 125.6 | 125.6 |
| 2 | HPMC E15 LV | 2000 | 1700 | 1500 | 1000 | 800 | 600 | 500 |
| 3 | PEG 400 (mL) | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 4 | Saccharin sodium | 220 | 220 | 220 | 220 | 220 | 220 | 220 |
| 5 | Cross carmelose Sodium | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| 6 | Citric acid | 80 | 80 | 80 | 80 | 80 | 80 | 80 |
| 7 | Tartaric acid | 80 | 80 | 80 | 80 | 80 | 80 | 80 |
| 8 | Menthol | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| 9 | Colour | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| 10 | Water (mL) | 12 | 12 | 10 | 10 | 10 | 10 | 8 |

*(All the quantities are in mg)

**Table 3. Taste masking of drugs using different sweetening agents.**

| S. No. | Ingredients | S1 | S2 | S3 | S4 | S5 | S6 |
|---|---|---|---|---|---|---|---|
| 1 | Dextromethorphan | 125.6 | 125.6 | 125.6 | 125.6 | 125.6 | 125.6 |
| 2 | HPMC E15 LV | 500 | 500 | 500 | 500 | 500 | 500 |
| 3 | PEG 400 (mL) | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 | 1.2 |
| 4 | Aspartame | 280 | - | - | - | - | - |
| 5 | Neotame | - | 280 | - | - | - | - |
| 6 | Perlitol 200 SD | - | - | 280 | - | - | - |
| 7 | Liquorice | - | - | - | 280 | - | - |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 8 | Sucralose | | | | | 280 | - |
| 9 | Aspartame | - | - | - | - | - | 280 |
| 10 | Cross carmelose sodium | 220 | 220 | 220 | 220 | 220 | 220 |
| 11 | Citric acid | 120 | 120 | 120 | 120 | 120 | 120 |
| 12 | Tartaric acid | 120 | 120 | 120 | 120 | 120 | 120 |
| 13 | Menthol | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| 14 | Colour | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| 15 | Water (mL) | 8 | 8 | 8 | 8 | 8 | 8 |

**Table 4. Taste masking of drug using Ion Exchange Resin.**

| S.No. | Ingredients | R**1** | R**2** | R**3** | R**4** |
|---|---|---|---|---|---|
| 1 | Dextromethorphan | 125.6 | 125.6 | 125.6 | 125.6 |
| 2 | Kyron T111 | 188.4 | 376.8 | 376.8 | 376.8 |
| 3 | HPMC E15 LV | 500 | 500 | 700 | 800 |
| 4 | PEG 400 (mL) | 1.2 | 1.2 | 2 | 2 |
| 5 | Cross Carmellose sodium | 220 | 220 | 220 | 220 |
| 6 | Aspartame | 260 | 260 | 260 | 260 |
| 7 | Citric acid | 120 | 120 | 120 | 120 |
| 8 | Tartaric acid | 120 | 120 | 120 | 120 |
| 9 | Menthol | - | 0.02 | 0.02 | 0.02 |
| 10 | Water (mL) | 8 | 8 | 8 | 8 |

Different amount of HMC E15 LV was taken and observed for their effect on mouth dissolving time. As the concentration of HPMC E15 LV polymer increases, mouth dissolving time is also increases respectively. From all the batches H7 batch was shown less mouth dissolving time is 16 sec. Mouth dissolving time data are shown in Table 6.

**Table 6. Mouth dissolving time of film containing different amount of HPMC E15 LV.**

| S. No. | Evaluation parameter | H1 | H2 | H3 | H4 | H5 | H6 | H7 |
|---|---|---|---|---|---|---|---|---|
| 1 | Mouth dissolving time (sec) | 118 | 80 | 80 | 58 | 29 | 23 | 16 |

Various types of sweeteners were tasted for their effective taste masking capacity Table 7. Among all the sweeteners, taste masking of drugs occurs with Neotame. The film was pleasant in taste and menthol helps to complete suppressant of remaining bitterness. It gives cooling effect after consumption. Taste masking is also done with Aspartame but after 5-10 min it tastes slightly bitter. Saccharin sodium, liquorice and sucralose are not sufficient to mask the bitterness of drugs.

**Table 7. Sweetening capacity of various sweetening agents.**

| Evaluation parameter | Saccharin sodium | Neotame | Perlitol | Liquorice | Sucralose | Aspartame |
|---|---|---|---|---|---|---|
| Sweetening capacity | Average | Average | Not done | Not done | Average | Good |

Drug and Ion Exchange Resin (Kyron T111) complex was tried to complete masking of bitter taste of drugs. Drugs and polymer ratio was taken 1:1 and 1:2. R1 and R2 batches was shown good masking of the taste but the problem occur with the folding endurance of the film. Films were easily broken. R3 batch was shown all the satisfactory parameters.

## Evaluation of Fast Dissolving Film

### Weight variation

Five films of each 2 square inch were cut at five different places from casted films and weight variation was measured. Weight variation varies from 85.99 ± 1.00 to 97.96 ±2.05 mg.

### Thickness of the film

The thicknesses of the drug loaded films were measured with the help of screw gauge. The thickness of film varies from 1.5±0.2 to 2.2 ± 0.1 mm.

### Folding endurance of the films

The folding endurance was measured manually. A strip of film 2 cm2 was cut and subjected for the folding endurance studies until it broke at the same place.

### In vitro disintegration time

A size of two square inch film was subjected for this study. The formulation H7 shows 16 sec (disintegration time).

### Mouth dissolving time

The mouth dissolving time was determined by using petridish containing phosphate buffer pH 6.8. A size of two square inch film was subjected for this study.

### % Drug content

The prepared film formulations were analyzed for % drug content and it was observed that all the formulation found to contain more than 95% drug content.

### In vitro dissolution studies

Dissolution of strip was taken in 300 mL of the medium containing 6.8 pH phosphate buffer. It was shown that within 30 min all the drugs were released the results are depicted in the figure 3.

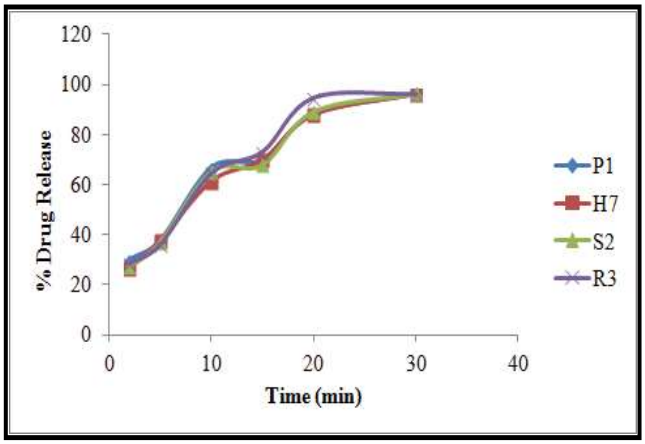

Figure 3. In vitro dissolution studies

## Short term stability study

The findings of a study on short-term stability indicate that the formulations' appearance and medication content have not changed significantly. Additionally, it was found that the formulations' mouth dissolving times were not significantly impacted.

## Conclusions

Without using any organic solvents, fast-dissolving films were created using the solvent casting technique. The FTIR study verified that dextromethorphan and both medications were compatible with the polymer (HPMC E15 LV). When the weight fluctuation and thickness of four films (P1, H7, S2, R3) were examined, the results were excellent. Due to the polymer's higher elasticity, the folding resistance of the films rose as polymer concentration increased. As more fluid is needed to moisten the film in the mouth, the mouth dissolving and film disintegration times grew longer as the polymer concentration increased. Aspartame and an ion exchange resin were used to cover up the film's unpleasant taste. According to a study on drug content, fast-dissolving films contain more than 95% of medicines. According to an in vitro dissolution analysis, more than 96% of the medication was released within 30 minutes. The results of the current investigation suggest that all four films had satisfactory film parameters. Conclusion: Solvent casting can be used to cast fast-dissolving films containing dextromethorphan without using any organic solvents. Therefore, ignoring or being careless with organic solvent in a film that dissolves quickly is a possible strategy. Film containing sweetener had the desired properties for elderly and paediatric patients who have difficulty swallowing conventional dose forms, including needed thickness of 2 mm, folding endurance of more than 300 folds, mouth dissolving time of 17 seconds, and more than 96% of drug release within 30 minutes. Over 96% of medicines that were released within 30 minutes indicated that quick beginning of action had been accomplished. It helped with the painful throat issue. A revolutionary medicinal dose form for paediatric, geriatric, and general populations could be a fast-dissolving film.

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