RESEARCH ARTICLE

Design, Development and Characterization of Ropinirole Mouth Dissolving Film by using Spin Coating Technique

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ABSTRACT

The aim of the research was to develop a ropinirole mouth-dissolving film employing solvent casting and spin coating methods with sesbenia gum acting as a film-forming agent. Parkinson's disease is treated with ropinirole. Sesbenia gum was designed as a film-forming ingredient in the 25 to 600 mg concentration range for solvent casting and 50 to 250 mg for spin coating. For both procedures, the concentration of the plasticizer propylene glycol was optimized between (0.3 and 1.0 mL). Film-forming agent and plasticizer effects at various concentrations were examined. For the solvent casting and spin coating processes, the plasticizer concentration was 0.3 mL for each, while the optimal film-forming agent concentrations were 50 and 150 mg, respectively. Ropinirole MDFs were made employing an enhanced concentration and more excipients. In comparison to the solvent casting approach, the spin coating process produced films with better surface morphology, a 24 seconds shorter disintegration time, good tensile strength of 3.2 (N/mm^2), a thinner thickness of 0.2 mm, and a maximum drug content of 93.14%. Sesbenia gum has been discovered to have greater potential for the spin-coating method of developing a ropinirole mouth-dissolving film.

Keywords: Sesbenia gum, Ropinirole, Mouth dissolving film, Solvent casting and spin coating method.

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INTRODUCTION

For most therapeutic agents, administration through the mouth has been considered the most convenient and well-liked delivery method. Over the past few decades, researchers have been working on developing intraoral delivery systems (IODS) that can provide the ideal drug exposure for the optimum therapeutic benefit. In order to provide those who had trouble in swallowing tablets, capsules and syrup, with an alternative to these traditional solid dosage forms, in the late 1970s, the first fast-dissolving drug delivery system was developed. The problem of swallowing solid dosage forms can be resolved with new and innovative oral drug delivery system, which swiftly dissolves in the mouth in a few seconds without water. Tablets, granules, pills, caplets, films, wafers and powders are part of fast and quick dissolving system. The tongue's top or bottom is where the film is placed. It maintains the application site while rapidly releasing the active ingredient for local and/or systemic absorption.[1]

A novel oral fast-dissolving dose form combines the convenience of dosing without water or beverage with the simplicity of administration. Despite their quick disintegration/dissolution times, some patient groups still worry about swallowing solid pills and run the danger of choking. Fast-dissolving film eliminated The possibility of choking.[2] Oral films can be divided into the following three categories.[3]

- Mucoadhesive sustained release wafers,
- Mucoadhesive melt away wafers and
- Flash release

Fast-dissolving film criteria: A good oral film should melt or disintegrate in mouth in few seconds without being swallowed, and it should work effectively for flavor masking. There should be no little residue left in the mouth on oral intake. Environmental variables, including humidity and temperature, have minimal effects on oral fast-dissolving film.

Ropinirole is used to treat Parkinson's disease and the symptoms of restless legs syndrome. The production of oral films involves the rolling method, hot melt extrusion, solid dispersion, semisolid casting, and solvent casting. The current investigation used spin coating and solvent casting to produce the oral film for the drug ropinirole.[3]

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MATERIALS AND METHODS

Materials

Ropinirole was purchased from Wokhahrtz Ltd. in Aurangabad, M.S., India. Sesbania, saccharine, propylene glycol, citric acid, and the flavor of a pineapple were purchased from Vinayak Industries Ltd. in Mehsana Ahamdabad, Gujarat, Merck in Mumbai, India, Rankem in Mumbai, India, Loba Chemicals in Mumbai, India, and Devansh Warehouse Pvt. Ltd. in Pune, respectively. Additional ingredients/chemicals were of the analytical and lab grade.

Methods

Mouth dissolving film- preparation by solvent casting method

In order to completely dissolve the gum in water, water-soluble polymer (SG) were dissolved in boiling distilled water (100°C) for 6 to 8 hours. The polymer solution was then cooled, filtered via a vacuum filter, and then added propylene glycol as a plasticizer. In beaker (A), the drug is combined with additional excipients after being dissolved in distilled water. Saccharine is added as a sweetener and citric acid as a saliva stimulant. Then, add the drug solution (A) to the polymer solution (B), keeping the mixture constantly stirred. The mixture was then cast into modified solvent casting plates[4] at 50°C dried in a hot air oven for 24 hours,[5] and cut into 2X2 cm pieces before being stored in well-closed container in dry condition (Table 1).

Moth dissolving film – Preparation by spin coating

Spin coating technique employed for the thin film preparation. In this procedure, the substrate is spun quickly from low to high speed with a small droplet of fluid resin placed to the center. The final film thickness and other properties will depend on the kind of resin used with viscosity, drying rate, percent solids, surface tension, etc. and the spin process parameters used. The number of water-soluble polymers used in ropinirole MDF preparation process were dissolved in boiling distilled water at a temperature (100°C) for 6 to 8 hours to completely solubilize the gum in water. Then propylene glycol was added to the polymer solution. Lastly, the preparation was cooled and dried in a vacuum. The drug is dissolved in distilled water, and then various excipients are added to the drug solution in beaker (A), including saccharine as a sweetener and citric acid as a saliva stimulant. The solutions were stirred with a magnetic stirrer and before coating the film with a spin coater, viscous liquids were sonicated up to the bubble-free solution. The typical process involves dripping a small amount of a viscous solution onto the center of a substrate and then rapidly spinning the substrate. (Generally, at 1500 rpm). The prepared substrate and film were heated to 450°C by using hot air oven for 2 hours. After two hours, the prepared film was peeled off of the substrate (Table 2).

Evaluation of Ropinirole MDF

In-vitro disintegration test

In order to conduct the *in-vitro* disintegration investigation on all Ropinirole MDFs, 10 mL of water heated to 37°C was put in a petridish with a diameter of 10 cm. Each MDF was then carefully placed in the centre of petridish, and the time it took to totally disintegrate was recorded.[6]

Weight variation

The uniformity of the weights of the formed films was examined. The average weight of ten films was determined after each one was weighed. The average weight was used to compare the different film weights.[6]

Thickness

The thickness of the film was measured using a digital vernier caliper (Mitutoyo, Japan) having a range of 0 to 10 mm and a resolution of 0.01 mm. The MDF sample, which matched the drug's dosage, was taken. MDF samples reading on the dial was recorded. Three measurements were averaged to find the mean thickness.[7]

Drug content uniformity

Twenty preparations were used to evaluate the uniformity of dosage content and amount of ropinirole was measured in each preparation by using Shimadzu- 1800 UV/VIS spectrophotometer. In USP27, Relative Standard Deviation must be below or equal to 6.0%, and the contents of the preparation's main component must lie within the 85 to 115% range.

Tensile properties: Tensile strength

Two tensile grips were fixed one to the base of the texture analyzer and the other to the load cell in order to measure the film's tensile strength. The sample was sandwiched between the two tensile grips. The highest force required to break the sample was taken into consideration, and the following equation was used to determine the tensile strength.[8]

$$Tensile\ strength = \frac{Rupture\ force}{Thickness \times width}$$

Percentage elongation

Strain is stretching when tension is applied to a strip sample. In general, strip elongation rises as plasticizer content does.[9]

$$\%\ 'Elongation' = \frac{Increase\ in\ length\ of\ strip}{Initial\ length\ of\ strip} \times 100$$

Folding endurance

Table 1: Formulation of ropinirole MDF by solvent casting method

Batch no.	*ROP (Mg)*	*SG (mg)*	*P.G. (mL)*	*Citric acid (mg)*	*Pineapple flavour (mL)*	*Saccharine (mg)*	*Methanol (mg)*	*D. W. (mL)*
A1	40	200	0.3	2.2	0.5	2.5	12	10
A2	40	100	0.3	2.2	0.5	2.5	12	10
A3	40	50	0.3	2.2	0.5	2.5	12	10
A4	40	25	0.3	2.2	0.5	2.5	12	10

Table 2: Formulation of ropinirole MDF by spin coating method

Batch no.	*ROP (Mg)*	*SG (mg)*	*P.G. (ml)*	*Citric Acid (mg)*	*Pineapple flavor (ml)*	*Saccharine (mg)*	*Methanol (mg)*	*D. W. (ml)*
B1	40	250	0.3	2.2	0.5	2.5	12	10
B2	40	150	0.3	2.2	0.5	2.5	12	10
B3	40	50	0.3	2.2	0.5	2.5	12	10

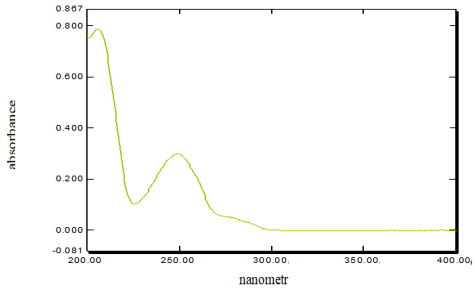


Figure 1: UV spectrum of ropinirole

Folding endurance is determined by repeatedly folding the strip in the same place till the strip breaks. The total number of folds a film can endure before breaking is used to compute its folding endurance value.

In-vitro dissolution test

The USP paddle technique used to determine the *in-vitro* dissolution test of all ropinirole MDFs in a dissolving device (Electrolab TDT-08L plus). All experiments were carried out in phosphate buffer of pH 6.8. The temperature was maintained at 37°C for dissolving media, and the paddle rotated at 50 rpm speed. Aliquots (5 mL) were periodically withdrawn at 5 seconds intervals, and dissolving media were added in the same quantity. Sample were analyzed spectrophotometrically (Shimadzu 1800) at a maximum wavelength of 249.50 nm. From the calibration curve, drug concentrations were determined.[10,11]

SEM study

SEM were used to examine the surface morphology of MDF with a magnification of X 25,000 (JEOL 5400, Tokyo, Japan).

RESULTS AND DISCUSSION

UV Spectroscopy

In distilled water, ropinirole (100 mg) was dissolved in concentrations range from 2 to 10 gm/mL, and its UV spectrum was seen at wavelengths between 400 and 200 nm (Figure 1). These peaks resemble the expected peaks, confirming the sample drug's identification as ropinirole. Ropinirole's reported absorbance maxima were at 250 nm.

Differential Scanning Calorimetry Study

Pure drug's DSC thermogram (Figure 2) demonstrated a clear endothermic peak at 243.430c. No physical or chemical instabilities were present since there was no peak or shift in the DSC thermograms.

FTIR Spectroscopy

The FTIR spectra (Figure 3) show that the sharp peak at 3074.53 cm^{-1} confirms primary amide group. The peak at

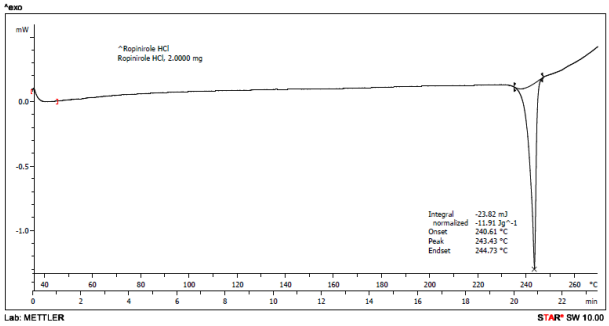


Figure 2: DSC thermogram of ropinirole

1614.42 cm^{-1} confirms C=C stretching, and peak at 1454.33 cm^{-1} confirms - CH3 starching in the drug's structure shown in Figure 3 and Table 3.

According to the Sesbenia gum's FTIR spectra, the peak 1645.28 proves the existence of C=C, two closer peaks at 2926.01 and 2883.58 confirms aliphatic C-H group, and a wide peak at 3317.56 indicates hydroxyl -OH group were shown in Table 4 and Figure 4.

Melting Point

The drug's melting point was identified between 242 and 246°C, while the claimed norm was 243°C, which supports authenticity.

Drug-excipient Interaction Study

FTIR spectroscopy was used to identify the chemical interactions between active components and excipients. A study is conducted to assess the compatibility of the medicine and excipient.

Infrared Spectroscopy

Shimadzu 8400S FTIR spectrophotometer (Japan), were used in 400–4000 cm^{-1} range. It is evident from the observation that the peak in the pure drug form is stable in physical combination; very little moving of one group is seen, hence there is no evidence of drug interaction with the mixture's excipients Table 5 and Figure 5.

Standard calibration curve of Ropinirole

The calibration curve for ropinirole in distilled water was determined in concentration range 2.0–10.0 gm/mL. (Figure 6)

The calibration curve for ropinirole in phosphate buffer (pH 6.8), which was determined in concentration range of 2.0–10.0 gm/mL Figure 7.

Evaluation of Prepared MDF (Solvent Casting Method)

A conclusion drawn from analysis in (Table 6). A texture analyzer's tensile strength measurement shows a positive correlation with the film-forming agent concentration. Additionally, the films' %elongation and folding durability

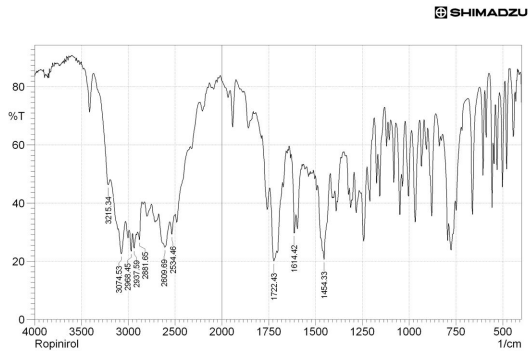


Figure 3: FTIR spectrum of ropinirole

Table 3: Ropinirole - functional groups

Functional group	*Range cm^{-1}*
-NH stretch	3074.53
-CH3 bend	1454.33
-C=O stretch	1722.43
-C=C- stretch	1614.42

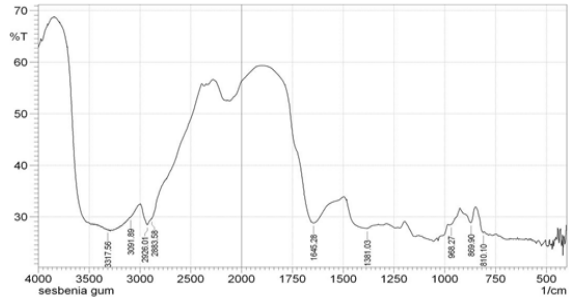


Figure 4: FTIR spectrum of sesbenia gum

Table 4: Sesbenia gum – functional groups

Functional group	*Range cm^{-1}*
C=C bend	1645.28
C-H aliphatic	2926.01, 2883.58
O-H stretch	3317.56

Table 5: FTIR study of physical mixture (Ropinirole + SG)

Functional group	*Observed peak in bulk (cm^{-1})*	*Peak in physical mixture(cm^{-1})*	*Inference*
-NH stretch	3074	3076	No interaction
-CH3 bend	1454	1454	No interaction
-C=O stretch	1722	1722	No interaction
-C=C- stretch	1614	1597	-

have decreased. According to IP, there is weight variation between the top and lower limits, hence the test is passed.

Evaluation of MDF prepared by spin coating method

According to the analysis in (Table 7), A texture analyzer's measurement of tensile strength shows a positive correlation with the film-forming agent concentration and the disintegration time. As the polymer concentration rises, the films'% elongation and folding durability likewise decrease. According

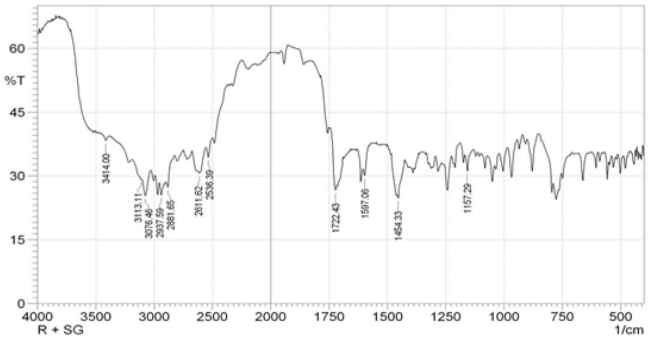


Figure 5: FTIR spectrum of physical mixture (Ropinirole + SG)

Table 6: Evaluation of MDF (Solvent casting method)

Batch	*D.T. (sec)*	*Tensile Strength (N/mm^2)*	*Thick ness (mm)*	*% elongation*	*Weight variation (mg)*	*Folding Endurance*
A1	43	1.22	0.4	100.59	8.1	140
A2	41	1.30	0.4	100.67	7.3	146
A3	38	2.41	0.4	104.9	7.8	199

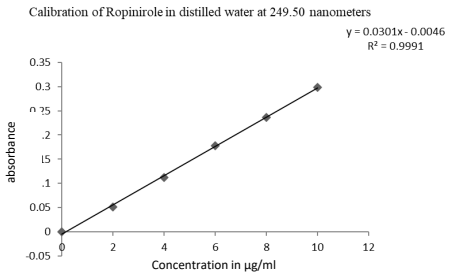


Figure 6: Calibration Curve of Ropinirole in distilled water

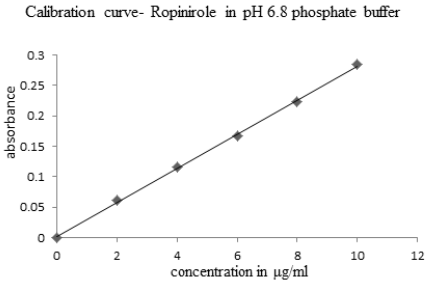


Figure 7: Calibration curve- ropinirole in pH6.8 phosphate buffer

Table 7: Evaluation of MDF for spin coating method

Batch No.	*D.T. (sec)*	*Tensile Strength (N/mm^2)*	*Thick ness (mm)*	*% elongation*	*Weight Variation (mg)*	*Folding Endurance*
B1	31	2.18	0.4	100.59	8.1	157
B2	24	3.2	0.4	110.55	7.5	204
B3	24	1.52	0.4	100.55	7.4	201

to IP, there is weight variation between the top and lower limits, hence the test is passed.

In-vitro Dissolution Study

The phosphate of pH 6.8 was employed as the solvent in an *in-vitro* dissolving investigation, which was conducted

using the dissolution test apparatus model number (Electrolab TDT 08L). The solvent casting method results reveal that the SG exhibits ideal film forming properties. An in-vitro dissolving investigation of optimized batches, as shown in (Figure 8) Casting A3, releases 91.0183% of the medication in 45 sec. spin coating technique (Figure 9) According to an *in-vitro* dissolution investigation of an optimized batch, coating B2-150 mg releases 93.1439% of the drug in 45 seconds, and the research's findings indicate that SG has strong film-forming properties and that spin-coated films release more medicine than films made with solvents casting method in the same time.

Surface Morphological Study

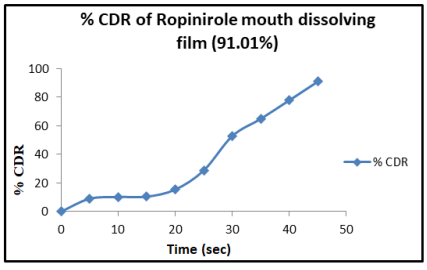
SEM was used to capture an image of oral MDF for morphological analysis at 500X magnification at 10 m lengths For MDF prepared by solvent casting method and 800X magnification at 20 m lengths for MDF prepared by spin coating method. The film had a gold coating, and the gold-coated images were scanned from the top. The resulting film, which contained ropinirole oral MDF, was not entirely clear and colorless. Solvent casting film, a drug with a smooth surface and some needle-like forms that are not fully dissolved was visible (Figure 10). It should be assumed that the entire drugs and excipients were not entirely and uniformly dispersed throughout the formulation because the scanned image also displays a clear image. There are fewer minor scratches in spin coating film (Figure 11) compared to solvent casting film.

Comparative Study of MDF by Both Methods

By using spin coating and solvent casting techniques, Ropinirole MDFs were developed. On the basis of the physical characteristics and tensile qualities reported in (Table 8), formulation batches were made and assessed. When these two methods were contrasted based on the analysis and

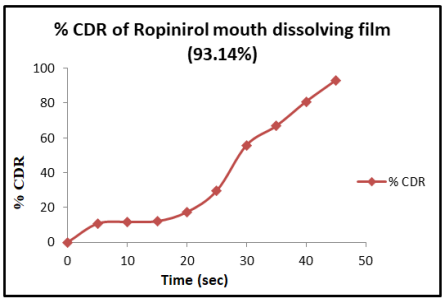
Table 8: Proportional study of ropinirole MDF

Evaluation parameter	*Solvent casting method (A4)*	*Spin coating technique(B3)*
Disintegration Time	38 sec	24 sec
Tensile strength	2.39 (N/mm^2)	3.2 (N/mm^2)
Thickness	0.4 mm	0.2 mm
% 'Elongation'	104.9 %	110.55 %
Weight	7.8 mg	7.5 mg
Folding Endurance	199	204
Drug content	91.01 %	93.14 %



Time(sec)	% CDR
0	0
5	9.0139285
10	10.24455357
15	10.46830357
20	15.39080357
25	28.81580357
30	52.86892857
35	64.95142857
40	77.92892857
45	91.01830357

Figure 8: *In-vitro* dissolution study (solvent casting batch A3)



Time(sec)	% CDR
0	0
5	10.69205357
10	11.69892857
15	12.03455357
20	17.29267857
25	29.59892857
30	55.77767857
35	66.85330357
40	80.83767857
45	93.14392857

Figure 9: *In-vitro* dissolution study (spin coating batch B2)

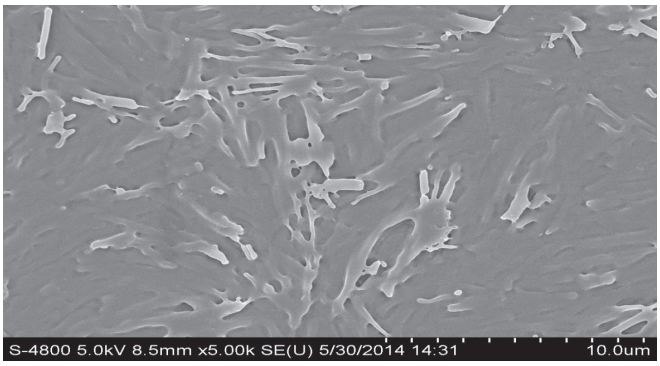


Figure 10: Image of ROP Solvent Casted MDF

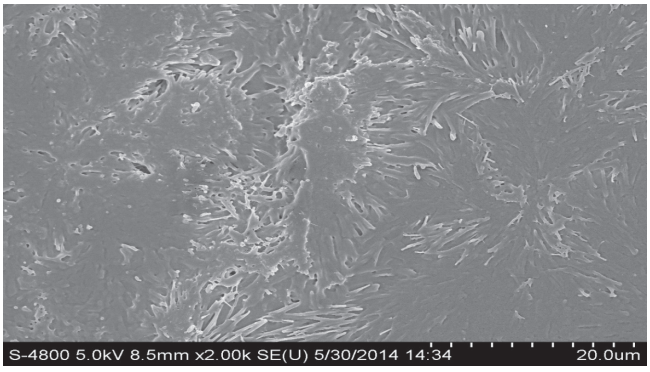


Figure 11: Images of ROP spin coated film

description of MDF. Because of its faster disintegration in 24 seconds, strong tensile strength- 3.2 N/mm^2, thinner thickness about 0.2 mm, maximum drug content about 93.14%, Lesser weight variation and improved fold durability, the spin coating technique is determined to be superior to the solvent casting approach. Although solvent casting is a highly common approach for creating mouth-dissolving films, it is only applicable in the laboratory; as a result, a unique spin coating technology with industrial application has been developed.

CONCLUSION

The solvent casting procedure was used to develop the mouth-dissolving film containing ropinirole sesbenia gum polymer is utilized in the spin coating technique as a film-forming agent. Sesbenia gum exhibits film-forming ability the best. Considering that it demonstrated film-forming capacities of (50 mg) for solvent casting method and (150 mg) for spin coating. Increase the amount of film that is screened to lengthen

disintegration and tensile strength times. As a consequence, using the right amount of film former and plasticizer will produce the greatest results. Increasing plasticizer concentration, which results in soft film but also longer film disintegration and dissolution times, improved tensile strength and %elongation. According to the investigation, the plasticizer PG is superior in terms of peeling ability and turning off disintegration and dissolving time. Therefore, plasticizer (PG) has enough tensile strength, percentage elongation, and short disintegration and dissolution times. Film is more fragile and easier to break without plasticizer in both ways. In light of this, it can be said that the formulation of the ropinirole mouth dissolving film was effective, and it has a bright future as a fast-acting drug delivery method.

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