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Hydrogel of Octopirox Using Different Polymers

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ABSTRACT

The purpose of the present study is to formulate a topical hydrogel for antifungal drug octopirox. This topical hydrogel was developed to allow the delivery of octopirox to the skin in high concentration and to limit its delivery through the skin. Different hydrogels were prepared, namely, Chitosan derivative, Carbopol-940, tamarind seed powder hydrogel. The influence of hydrogel type on their rheological properties, pH-values, in-vitro drug release studies was investigated. The best release results were obtained for the hydrogel prepared with chitosan derivative hydrogel and carbopol-934 which also showed suitable rheological properties for use as a vehicle for topical drug delivery. Therefore, chitosan derivative and carbopol hydrogel can be considered as a promising topical antifungal system.

INTRODUCTION

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal, skin as topical routes. Skin is one of the most readily accessible organs of the body for topical administration and is the main route of topical drug delivery system. In recent years scientific and technological advancement had been made in the research and development of hydrogel drug delivery systems by overcoming physiological adversities such as the metabolism and for improved local action. Several approaches are currently utilized to treat pain, inflammation, skin diseases and as controlled release devices in the field of a dressing. Research studies were carried out on the formulation of transdermal hydrogels of antifungal agents by using various polymers. Octopirox is an antifungal medication, which prevents fungus from growing on the skin. Topical medication is used to treat skin infections such as athlete's foot, jock itch, ringworm, and yeast infections. Blending of chitosan with other polymers and effective methods of improving the physical and mechanical properties of chitosan for practical applications. The objective of the study is to determine the effect of different polymer and chitosan derivative as a topical gel formulation to form hydrogel as a controlled release vehicle containing octopirox by in-vitro drug release evaluation.

MATERIALS AND METHODS

Materials

Chitosan was procured from Mytsa Fisheri Technology Cochin. Octopirox gift sample from Clarient Pharmaceuticals Mumbai, India. Carbopol-934 was purchased from Zim Lab Nagpur. Tamarind seeds powder purchased from the local market. All the other reagents used were of analytical grade.

Methods

Preformulation study

Organoleptic Characteristics

The drug was evaluated for its appearance, melting point, solubility studies and partition coefficient.

Solubility

The Octopirox was found to be soluble in most of the organic solvents (methanol, ethanol) and was poorly soluble in distilled water showing its hydrophobic nature.

Determination of λmax

The isolated Octopirox was dissolved in methanol and its UV absorption spectrum was compared with standard Octopirox. Spectrophotometric analysis was carried out in Shimadzu 1800 UV spectrophotometer.

Calibration curve of octopirox in pH 7.4 phosphate buffer and methanol (9:1)

Various drug concentrations (2-20µg/ml) in phosphate buffer pH 7.4 were prepared and the absorbance was measured at 209 nm. For the standard graph, Octopirox 100mg was dissolved in a small amount of methanol and the volume was made up to 100ml using phosphate buffer pH 7.4. From this stock solution 10ml was withdrawn and diluted to 100ml with phosphate buffer pH 7.4. From this stock serial dilutions were made and pipette out 2,4,6,8,10,12,14,16,18 and 20ml and diluted upto 100ml with phosphate buffer pH 7.4 to obtain the solutions of concentrations ranging from 2-20µg/ml. The absorbance was measured at 309 nm using a spectrophotometer.

IR Spectroscopy

The spectrum was recorded in the wavelength region of 4000 to 400 cm-1. A dry sample of the drug and potassium bromide were mixed uniformly and filled into the die cavity of the sample holder and an IR spectrum was recorded using diffuse reflectance FTIR spectrophotometer.

Screening of polymers

Preformulation studies were carried out using polymers like HPMC E5, HPMC E15, Chitosan derivative, Eudragite L-100, and Grade of Carbopol-940, Carbopol-971, Carbopol-974, Carbopol-934. Chitosan derivative, carbopol-934, and Tamarind seeds powder. Combination of Carbopol-934. Chitosan derivative, carbopol-934, and Tamarind seeds powder. Was also which shown results therefore it was considered in formulation studies.

Development of hydrogel Formulation bases

Carbopol hydrogel

Carbopol- 934 was dispersed in water and kept under magnetic stirring for 12 hr. few drops of triethanolamine (TEA) were then added for neutralization and allow to settle down for gel formation. After that, the gel was stirred at room temperature for 24 h.

Chitosan hydrogel

Powdered chitosan was dissolved in 100 ml of 10% (w/w) citric acid solution, and sonicated for 10min and keep a side for overnight.

Tamarind seed powder hydrogel

Powder of tamarind seeds was dissolved in hot water, stirred for 1hr. and kept overnight for swelling. Further added to other excipients.

Table 1: Composition of Hydrogel of Octopirox

Formulation Batches	Octopirox (g)	Chitosan derivative (g)	Carbopol-934 (g)	Tamarind seed powder (mg)	Methyl Paraben (g)	Water (g)
F1	0.5	3.0	3.0	-	0.5	Upto 100
F2	1.0	3.0	3.0	-	0.5	Upto 100
F3	1.5	3.0	3.0	-	0.5	Upto 100
F4	2	3.0	3.0	-	0.5	Upto 100
F5	0.5	-	3.0	3.0	0.5	Upto 100
F6	1	-	3.0	3.0	0.5	Upto 100
F7	1.5	-	3.0	3.0	0.5	Upto 100
F8	2.0	-	3.0	3.0	0.5	Upto 100
F9	0.5	3.0	-	3.0	0.5	Upto 100
F10	1	3.0	-	3.0	0.5	Upto 100
F11	1.5	3.0	-	3.0	0.5	Upto 100
F12	2	3.0	-	3.0	0.5	Upto 100

Evaluation of Hydrogel

Appearance

The formulated hydrogels were observed for their visual appearance, color, texture, feel after application for grittiness, greasiness, stickiness, smoothness, stiffness, and tackiness.

Measurement of pH

The pH of various gel formulations was determined by using a digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation is done in triplicate and an average value was calculated.

Drug content

1 g of the prepared gel was mixed with 100ml of a suitable solvent. Prepared dilution of concentration 10µg/ml and analyzed at ƛmax 309nm by UV spectrophotometer absorbance method. Drug content was calculated using the equation, which was obtained by linear regression analysis of the calibration curve.

Viscosity

The viscosity of formulated hydrogels were determined using Brook-field viscometer (spindle number-7) in triplicate and the average of three reading was recorded.

Spreadability

It was determined by wooden block and glass slide apparatus. About 20g was weighed and added to the pan. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from hydrogel placed between, under the application of a certain load. Lesser the time taken for the separation of two slides, resultant better the spreadability. Spreadability was then calculated by using the formula:

$$S = M \times L / T$$

Where,

S = Spreadability

M = Weight tide to upper slide

L = Length of glass slide

T = Time taken to separate the slide completely from each other (Unit =g.cm/sec)

In-vitro Drug Diffusion

In-vitro diffusion profile of the hydrogel was determined by using Franz diffusion cells. Dialysis membrane with a 2.2 cm^2 diffusion area was used as a barrier. The diffusion studies were carried out at 37 ºC using pH 7.4 phosphate buffers as (receptor phase) diffusion medium. 1 gram of the gel of each formulation was exposed to diffusion study and samples were withdrawn at different time intervals such as 1, 2, 3,4,5,6,7,8,9 and 10 hr with the addition of equal amount of same fresh buffer solution to keep the volume constant. The samples were analyzed by a UV spectrophotometer at 309 nm and the amount of drug released was determined from a previously calculated standard curve.

RESULTS AND DISCUSSION

Physical characterization of Octopirox

Table 2: Physical characterization of Octopirox

Experimental	Property Studied	Result
Organoleptic property	Color	White
	Odour	Odorless
	Taste	Slight bitter
	Nature	Hydrophilic
Identification of drug sample	Melting point	138

IR Spectroscopy to predict the Compatibility of a carbopol 934, tamarind seed powder, chitoson with a drug IR study was carried out to check the compatibility between the selected excipients and Octopirox. The spectra obtained for I.R studies at a wavelength from 4000 cm-1 to 400 cm-1. After interpretation it was confirmed that there were no major shifting as well as no loss of functional peaks between the spectra of the octopirox gelling agent, physical mixture of drug and gelling agent From the I.R studies it was concluded, that selected gelling agents are compatible with the selected drug octopirox.

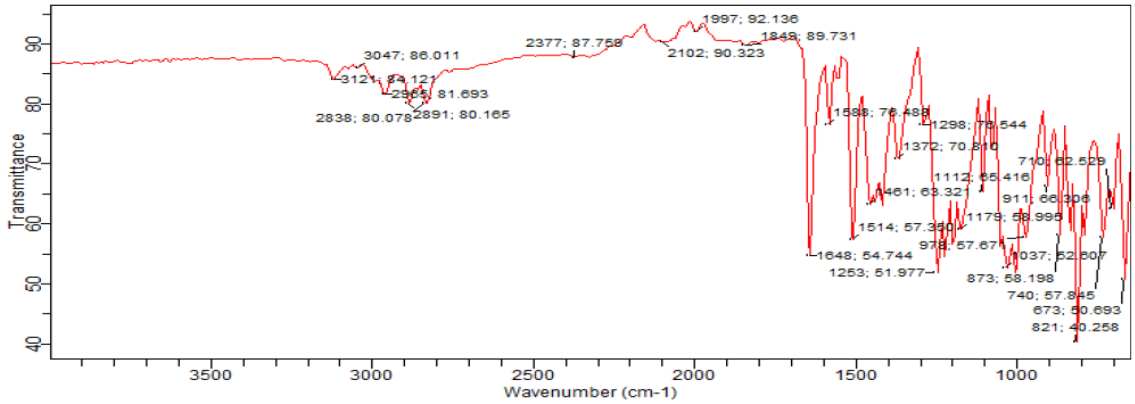


Figure 1: IR Spectrum of octopirox

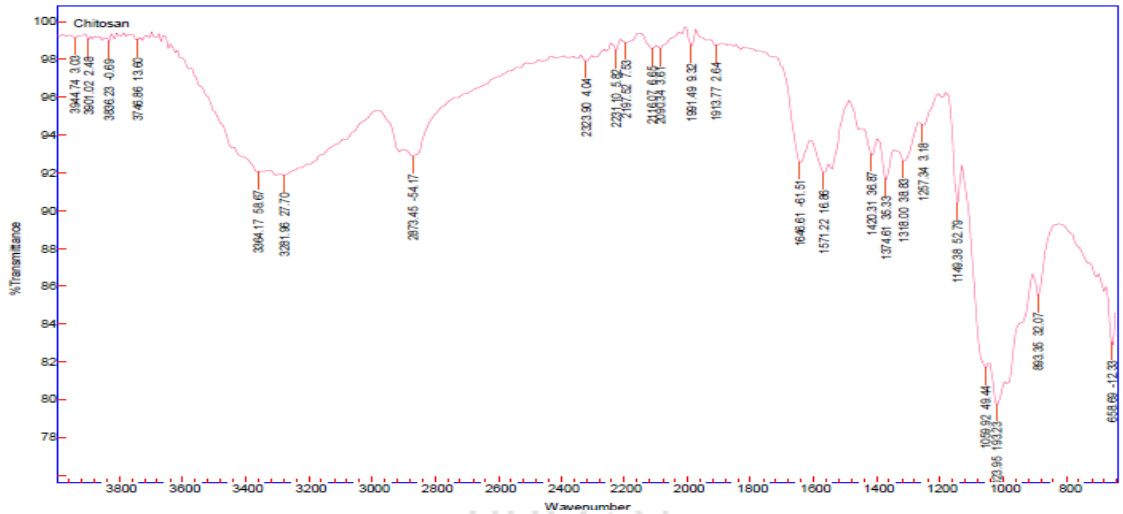


Figure 2: IR Spectrum of chitosan

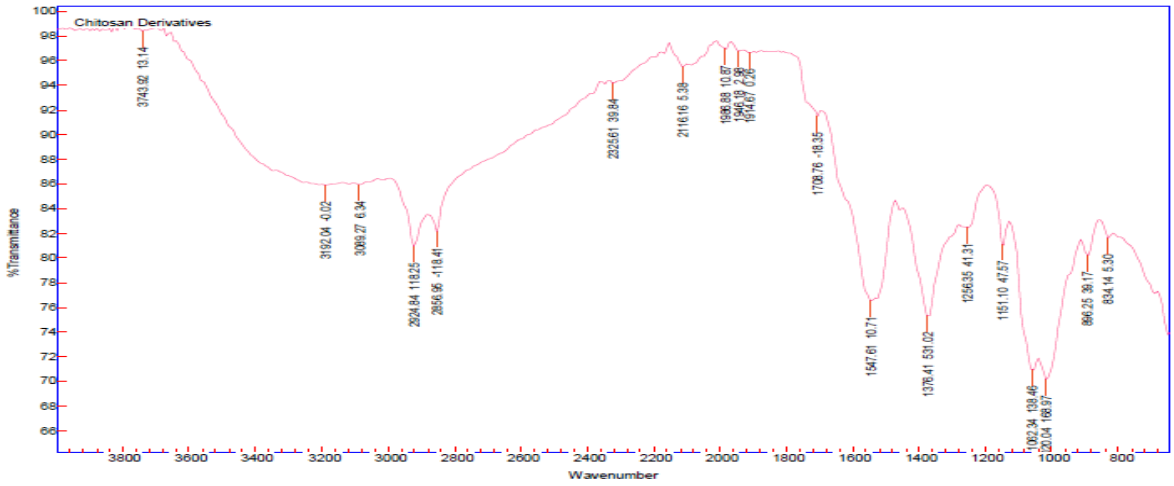


Figure 3: IR Spectrum of Chitosan Derivative

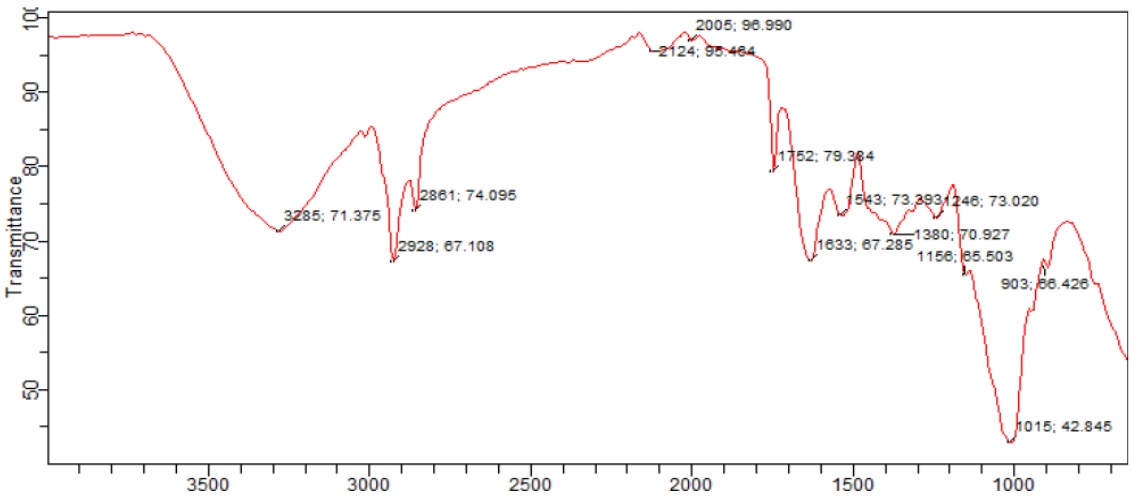


Figure 4: IR Spectrum of Tamarind seeds powder

Screening of polymers

Preformulation studies were carried out using polymers like HPMC E5, HPMC E15, Chitosan derivative, Eudragite L-100, and Grade of Carbopol-940, Carbopol-971, Carbopol-974, Carbopol-934. Chitosan derivative, carbopol-934, and Tamarind seeds powder. Combination of Carbopol-934, Chitosan derivative, carbopol-934, and Tamarind seeds powder. Showed satisfactory results therefore it was considered in formulation studies.

Evaluation of prepared Hydrogel

Physical appearance

The prepared Octopirox hydrogel were inspected visually for color, homogeneity, consistency. All formulations showed a white buff and yellowish color, glossy appearance. (Table 3)

Table 3: Colour, Feel on application, pH, Drug content, Spreadability

Formulation	Colour	Feel on application	Drug content (%)	pH	Spreadability
F1	white buff	Smooth	98.09	6.10	16
F2	white buff	Smooth	97.50	6.40	18
F3	white buff	Smooth	98.0	5.70	15
F4	white buff	Smooth	98.35	6.50	16
F5	Yellowish	Smooth	95.10	6.25	14
F6	Yellowish	Smooth	96.09	6.30	17
F7	Yellowish	Smooth	98.32	6.38	16
F8	Yellowish	Smooth	95.05	6.45	17
F9	Yellowish	Smooth	97.13	6.39	18
F10	Yellowish	Smooth	96.18	6.32	13
F11	Yellowish	Smooth	95.99	6.28	14
F12	Yellowish	Smooth	97.40	6.14	14

Measurement of pH:

The pH of hydrogen formulations was in the range of 6.0 to 6.50 which considered acceptable to avoid the risk of skin irritation upon application to skin shown in table 3.

Drug content:

The results of drug content are shown in table 2. The drug content of different hydrogel was estimated and the results were in the official limit if the range of 95.99-98.32 % which show uniform distribution of the drug throughout the hydrogel.

Spreadability studies:

All the formulations developed were checked for the spreadability. All the formulation showed spreadability between 13-18. The results of various formulations are given in table 2.

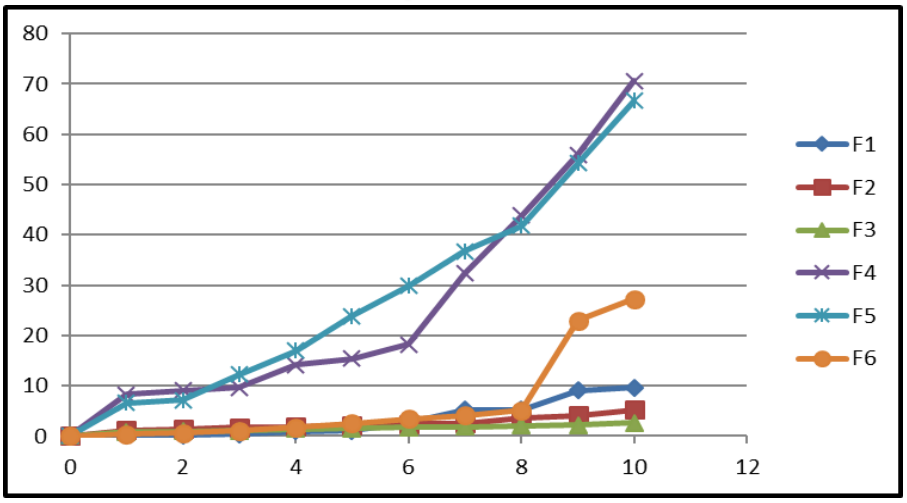
In-vitro drug Release:

The in-vitro release of Octopirox from different hydrogel formulations at 37ºC was investigated and the results are represented in figure. It was noticed that the release Octopirox

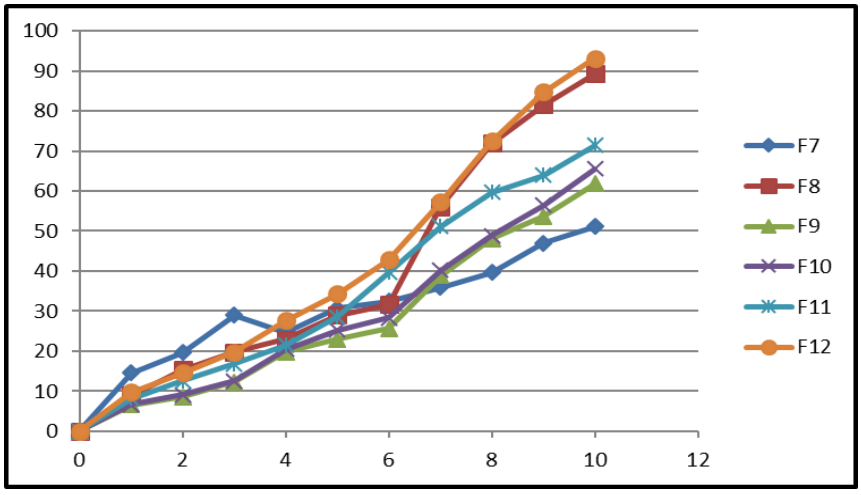
from its hydrogel can be shown less release further increase the concentration of drug also increase in drug release.

Table 4: % Drug release of F1-F12

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	0.0	1.2	0.79	8.3	6.6	0.38	14.5	9.0	6.5	6.7	8.2	9.8
2	0.17	1.4	0.91	9.1	7.2	0.59	19.6	15.4	8.5	9.1	12.5	14.5
3	0.39	1.8	1.08	9.6	12.3	1.11	29.0	19.7	12.3	12.6	16.8	19.7
4	0.91	1.9	1.42	14.2	17.0	1.7	24.7	23.0	19.8	20.4	21.5	27.7
5	1.08	2.2	1.48	15.4	23.9	2.5	30.7	29.0	23.0	25.3	28.6	34.3
6	2.60	2.4	1.70	18.2	29.9	3.4	32.4	31.7	25.6	28.3	39.7	42.9
7	5.2	2.5	1.82	32.3	36.7	4.1	35.9	56.0	38.9	40.2	51.1	57.2
8	5.3	3.6	2.05	43.8	41.8	5.1	39.6	72.0	48.0	48.8	59.7	72.5
9	9.1	4.1	2.16	55.9	54.2	23.0	47.05	81.5	53.6	56.4	63.9	84.8
10	9.6	5.2	2.6	70.6	66.6	27.3	51.19	89.35	61.8	65.6	71.4	93.2



Graph 1: %drug release of F1-F6



Graph 2: %drug release of F7-F12

CONCLUSION

Formulate and evaluate hydrogel using octopirox and different polymers. From the result obtained from the executed work it can be conclude that the drug and excipients were evaluated for confirmation. The drug content results help to conclude that the optimize batch having percent drug content within a range of 95.99 to 98.32% which show the uniform distribution of the drug throughout the hydrogel. When evaluate for spreadability, pH, and shown well consistency. When evaluated for the drug release of the optimized batch i.e. F1 to F12 was concluded that the drug release rate increases with its increasing concentration.

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