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Original Article

Design and Characterization of Periodontal Films of Moxifloxacin Hydrochloride by Using Basil Seed Gum

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ABSTRACT

The objective of this research was to design and evaluate site specific Periodontal strips containing Moxifloxacin hydrochloride (MH) in a biocompatible carriers which has excellent activity against wide range of microorganisms. To prepare MH periodontal films by using natural biocompatible polymer (Basil seed gum etc). BSG was extracted from Basil seeds. This will be used in preparation of periodontal strips. FT-IR has performed to reveal no interaction between MH, ISG and other excipients. The method choosen for preparation of periodontal strips is solvent casting technique. The prepared strips has to be evaluated for their thickness uniformity, folding endurance, weight uniformity, content uniformity, surface pH, and *in-vitro* antibacterial activity. *In-vitro* release from periodontal films has to fit to different equations and kinetic models like zero order, first-order equations and Hixson-Crowell, Higuchi models and korsmeyer peppas model to reveal drug release kinetics. A short-term stability study has to be performed to study the whether their will be decline in drug content or any changes in dosage form.

Keywords: Moxifloxacin hydrochloride, *In-vitro* release, Periodontal strip, Basil seed gum

1. INTRODUCTION

Periodontitis, i.e., "peri" = around, "odont" = tooth, "itis" = inflammation, refers to a number of inflammatory diseases affecting the periodontium, the supporting tissues around the teeth. Periodontitis involves progressive bone loss around the teeth, leads to the loosening and subsequent loss of teeth, and is characterized by periodontal pocket formation. The emergence of periodontal disease is from a pre-existing gingivitis. The inflammation of gingiva alone is termed gingivitis, and the severe inflammation of the periodontal structures with destruction of alveolar bone is called periodontal disease. Periodontitis is caused by

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microorganisms that adhere on the tooth's surfaces, along with an overly aggressive immune response against these microorganisms[1,2,3].

The invisible, sticky film called plaque mainly composed of bacteria stays on the teeth for more than two or three days, can harden under the gumline into tartar (calculus). Tartar makes plaque more difficult to remove and acts as a reservoir for bacteria[2,4,5]. Longer the plaque and tartar remain on the teeth, more the damage they cause. Initially irritation and inflammation occurs at the gingiva, which eventually causes pockets to develop between the gums and teeth that fill with plaque, tartar and bacteria. In time, these pockets become deeper and more bacteria accumulate, which causes infection and eventually leads to loss of tissue and bone[6,7,8].

Basil seed gum is used as a novel excipient in the present study. Basil (*Ocimumbasilicum* L.) is an annual herb that belongs to the family *Lamiaceae*[9].

2. MATERIALS AND METHODS

The following materials are used in the present work: Moxifloxacin Hydrochloride Aurobindho pharmaceuticals ltd, Acetic acid, Agar, Sodium hydroxide, Chitosan, Ethyl cellulose, Chloroform, Dibutyl Pthalate, Di-Sodium phosphate, Mono-sodium phosphate, Dibutyl phthalate (SD Fine chemicals, mumbai), Basil seeds. Etc.

Extraction of gum from Basil seeds

Mucilage was extracted using distilled water. 100 gms of Basil seeds were added to a specific proportion of distilled water at a desired temperature for 2 hours. The soaked seeds were blended for entire extraction period. Slurry was maintained at a constant temperature and continuously stirred using a magnetic stirrer. Later, mucilage was separated from seeds using a rubber spatula on a mesh screen. Slurry obtained was passed through a screen of 8 folds of muslin cloth. Separated mucilage was precipitated with equal amount of acetone. The precipitated mucilage was then separated and dried at 50°C for 10 h in a conventional hot air oven. Also, the adhered mucilage from the dried seeds was separated by rubbing them over a 40 mesh screen. The mucilage gum is collected and used as novel excipient.

The periodontal strips of moxifloxacin is to prepared by using solvent casting method by using the extracted Basil seed gum in 1:1 ratio and simultaneously same ratio drug and chitosan has to prepared and compared[9].

Standard curve of Moxifloxacin HCL

A calibration curve of Moxifloxacin HCL 2-10 mcg/ml of the drug in 1% v/v acetic acid in distilled water was constructed at a λ_{max} of 288nm using UV-VIS spectrophotometer (Shimadzu Corporation). Beer's law obeyed to construct the calibration curve in the concentration range of 2-10mcg/ml. Analyses were done in triplicate. The calculation of the drug release rate studies are based on the standard curve[11,12,13,14].

PREFORMULATION STUDIES

Prior to the development of the dosage form preformulation studies were carried out on parameters like melting point, Loss on drying, partition coefficient, viscosity of polymers, interference of polymers, interaction studies of drug and polymers.

1.Melting point determination: Melting point of drug was determined by taking a small quantity of drug in a capillary tube sealed at one end and was placed in melting point apparatus and temperature range at which the drug melts was noted.

2.Loss on drying: It was determined by drying 1 g of drug in an oven at 100-105^{0}C for 4 hours.

3.Partition coefficient determination: Take 5 ml of butanol in 50 ml volumetric flask and add drug to saturation. Then add 15 ml of phosphate buffer pH6.6 and keep it in a shaker bath for 24 h at 250˚C. Separate the aqueous layer and organic layer using separating funnel. Take 1 ml of aqueous solution and organic solution in a separate 25ml volumetric flasks. The absorbance of solutions was measured at 288 nm.

4.**Fourier transform infrared spectroscopy (FTIR):** The pure drug and polymers were subjected to IR studies alone and in combination. About 3 mg of pure drug/pure polymer/combination of drug-polymer were grinded with 97 mg of potassium bromide in a smooth mortar to affect through mixing.

PREPARATION OF PERIODONTALFILMS OF MOXIFLOXACIN BY USING SOLVENT CASTING METHODS

Basil seed gum/Chitosan/Ethyl cellulose (Different concentrations as per formula) was soaked in 100 ml aqueous acetic acid solution (1% v/v) for 24 hour to get a clear solution, which was later filtered through a muslin cloth. Moxifloxacin was incorporated in 100 ml of Basil seed gum/chitosan/Ethyl cellulose solution and vortexed for 15 min. The viscous dispersion was kept aside for 30 min for complete expulsion of air bubbles. Films were cast by pouring the drug-polymer solution into the center of glass moulds and allowed to dry at room temperature. The dry films were cut into strips of (5mm × 5 mm), wrapped in aluminum foil and stored in a calcium chloride desiccator at room temperature pending evaluation [8, 10, 11].

EVALUATION OF PHYSICAL PARAMETERS OF DRUG LOADED POLYMER STRIPS [12, 13, 14, 28-30]

Formulated films were subjected to the preliminary evaluation tests. Films with any imperfections, entrapped air, or differing in thickness, weight (or) content uniformity were excluded from further studies.

1. Thickness uniformity of the films: The thickness of each film was measured using screw guage (thickness tester) at different positions of the film and the average was calculated[12].

2. Uniformity of weight of the films: Film (size of 1 cm^2) was taken from different areas of film. The weight variation of each film was calculated.

3.Swelling index of the films: Films are weighed individually (designated as W1), and placed separately in 2% agar gel plates, incubated at 37°C ± 1°C, and examined for any physical changes. At regular 1-hour time intervals until 3 hours, films are removed from the gel plates and excess surface water is removed carefully using the filter paper. The swollen patches are then reweighed (W2) and the swelling index (SI) is calculated .[26]

4.Drug content uniformity of films: Drug content uniformity of films: Films size of 25 mm^2 were dissolved in10 ml of methanol in volumetric flasks. Keep the volumetric flask aside till the film is completely dissolved. Withdraw 1 ml solution in to a 25ml of volumetric flask then absorbance was measured at 288 nm by UV spectroscopy. The film size of 25 mm^2 without drug serves as a blank.

5.Folding endurance: The folding endurance of the films was determined by repeatedly folding one film at the same place till it broke or folded up to 300 times, which is considered satisfactory to reveal good film properties. The film was folded number of times at the same place without breaking gave the value of the folding endurance. This test was done on all the films for five times[26,27].

6.Surface pH: Periodontal films were left to swell for 1 hour on the surface of the agar plate, prepared by dissolving 2% (w/v) agar in warmed double distilled water under stirring and then pouring the solution into the petridish to gelling / solidify at room temperature. The surface pH was measured by means of pH paper placed on the surface of the swollen film. The mean of three readings was recorded[28].

7.In vitro drug release: Since the pH of the gingival fluid lies between 6.5 – 6.8, phosphate buffer pH 6.6 was used as simulated gingival fluid and the film remains immobile in the periodontal pocket, a static dissolution method was adopted for the dissolution studies. Sets of six films of known weight and dimension were placed separately into small sealed vials containing 2 ml of phosphate buffer. Thevials were kept at 37 ± 0.5 0C for 24 h, the 1 ml buffer was then drained off and replaced with a fresh 1 ml of buffer. The concentration of the drug was determinedand this procedure was continued for 4 consecutive days[29].

8.In vitro antibacterial activity: The films (25 mm^2) containing 15 mg of drug were taken for the study, 60 ml of nutrient agar media was prepared and sterilized at 15 lb pressure for 20 min in an autoclave. Under aseptic condition 20 ml of nutrient agar media was transferred into three sterile petri plates. After solidification 0.1 ml of microbial suspension of known concentration was spread on the media and incubatedat 37^0C for 72 hrs then the zone of inhibition was measured[28].

3. RESULTS AND DISCUSSION

Melting point determination: Melting point range of Moxifloxacin hydrochloride was found to be 238-242˚C.

Loss on drying: Not more than 5.0 per cent.

Partition coefficient determination: -0.508

Fourier transform infrared spectroscopy (FTIR): By the FTIR studies it is found to be there is no interaction between drug and excipients.

The following evaluation parameters thickness uniformity of the films, uniformity of weight of the films, tensile strength of the films, drug content uniformity of films, folding endurance and surface pH values are given in table No. 2 and *invitro* drug release in table no. 3, 4 and 5.

Thickness uniformity of the films: The thickness of each film was measured using screw guage (thickness tester) at different positions of the film and the average was found to be in the range of 0.35 mm ±0.01 to 0.46 mm ±0.04.

Uniformity of weight of the films: Film (size of 1 cm^2) was taken from different areas of film. The weight variation of each film was found to be in the range of53 mg ±5 to 63 mg ±4.

Swelling index of the films: The swelling index of the film was found to be 34.4 % ±0.03 to 48.2 % ±0.06.

Drug content uniformity of films: Drug content uniformity of films for different formulations were in the range of84 % ±0.17 to 97 % ±0.02.

Folding endurance: The film was folded number of times at the same place without breaking gave the value of the folding endurance240 to 310.

Surface pH: The surface pH was measured by means of pH paper placed on the surface of the swollen film. The mean of three readings was 6.1 to 6.7.

In vitro drug release: The In-vitro cumulative drug release for different formulations was found to be in the range of 83 to 95% after seven hours.

In vitro antibacterial activity: In vitro antibacterial activity studies showed that the prepared film inhibited growth of microbial colonies, this is detected by zone of inhibition.

Table 1:Formulation of periodontalfilms of Moxifloxacin hydrochloride

Formulation → Ingredients ↓	F1	F2	F3	F4	F5	F6	F7	F8	F9
Moxifloxacin Hydrochloride(mg)	120	120	120	120	120	120	120	120	120
Basal seed gum	-	-	-	-	-	-	300	400	500
Chitosan	-	-	-	300	400	500	-	-	-
Ethyl cellulose	300	400	500	-	-	-	-	-	-
Dibutyl phthalate(ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Alcohol(ml)	3	3	3	3	3	3	3	3	3
Chloroform(ml)	7	7	7	7	7	7	7	7	7

Table 2: Evaluations of Moxifloxacin hydrochloride periodontal films

Batch code	Thickness (mm)	Weight variation (mg)	Folding Endurance	Surface pH	Swelling Index %	Content Uniformity
F1	0.41±0.02	57 ±2	288	6.3	38.6±0.07	97±0.02
F2	0.42±0.03	54±2	280	6.2	41.8±0.06	86±0.02
F3	0.37±0.02	63±4	255	6.1	43.5±0.05	86±0.15
F4	0.46±0.04	62±5	263	6.4	44.3±0.04	86±0.03

F5	0.36±0.03	53±8	288	6.4	34.4±0.03	87±0.16
F6	0.43±0.04	58±4	310	6.5	36.4±0.04	84±0.17
F7	0.42±0.02	54±1	290	6.3	46.1±0.09	88±0.21
F8	0.39±0.13	53±5	246	6.6	48.2±0.06	87±0.23
F9	0.35±0.01	55±4	240	6.7	40.2±0.05	93±0.13

Table 3: Cumulative % drug release of Moxifloxacin hydrochloride periodontal films formulations F1-F3

Time (Hr)	F1	F2	F3
0	0	0	0
1	32	27	19
2	61	53	24
3	75	68	40
4	96	81	54
5		98	70
6			81
7			90

Table 4: Cumulative % drug release of Moxifloxacin hydrochloride periodontal films formulations F4, F5 and F6

Time (Hr)	F4	F5	F6
0	0	0	0
1	29	22	16
2	41	35	30
3	72	44	46
4	96	52	56
5		75	68
6		98	77
7			95

Table 5: Cumulative % drug release of Moxifloxacin hydrochloride periodontal lfilms formulations F7, F8 & F9

Time (Hr)	F7	F8	F9
0	0	0	0
1	35	29	16
2	55	43	33
3	78	59	40
4	96	78	56
5		98	60
6			78
7			95

Table 6: Kinetics data of Moxifloxacin hydrochloride periodontal films

Batch no	Parameters	Zero order	First Order	Higuchi	Hixson's crowell cube root
F6	R^2	0.94583	0.39114	0.822019	-0.52179
	K	1.045981	0.03047	7.954441	-0.04207
F9	R^2	0.95075	-0.904616	0.971305	-0.79091
	K	3.284714	-0.08137	5.489414	-0.12435

Table 7: Stability studies of Optimised formulations

Time in days	Physical changes
01	--
07	**No Change**
14	**No Change**
21	**No Change**

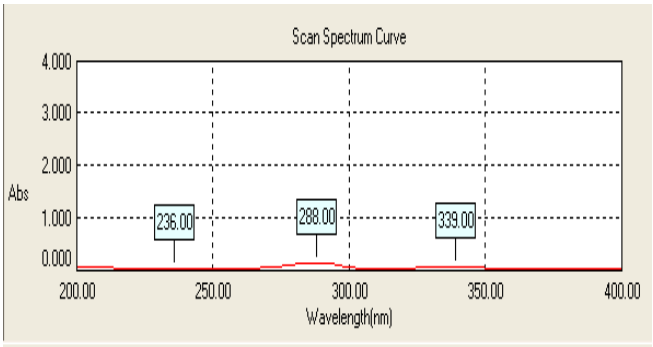

Fig 1: Scan spectrum of Moxifloxacin HCl

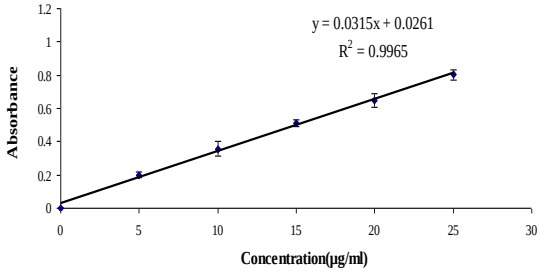

Fig 2:Standard plot data of Moxifloxacin Hydrochloride in phosphate buffer pH 6.5, λ_{max}= 288 nm.

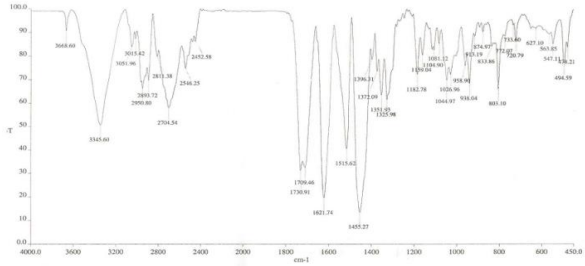

Fig 3: Infrared spectrum of Moxifloxacin hydrochloride

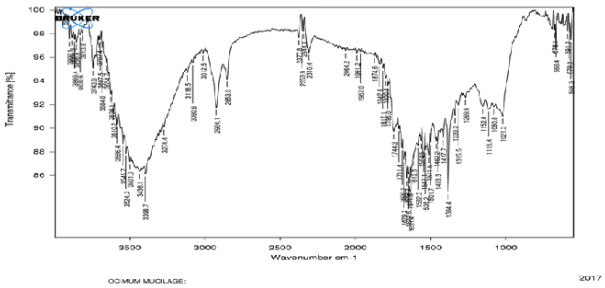

Fig 4: Infrared spectrum of Basil seed gum

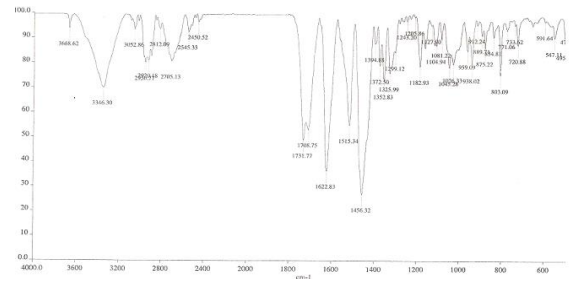

Fig 5: Infrared spectrum of Moxifloxacin hydrochloride and Basil seed gum

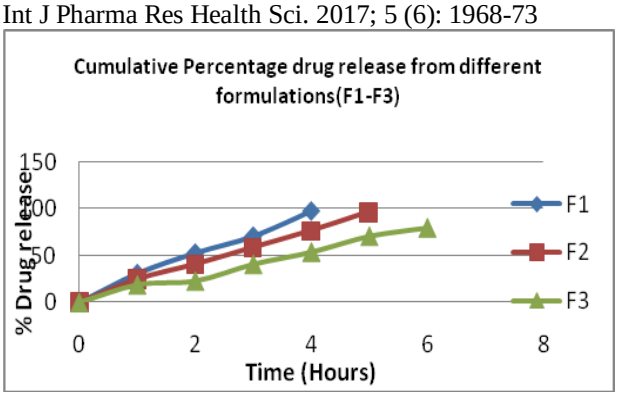

Fig 6: Cumulative % drug release of Moxifloxacin hydrochloride periodontal films formulations F1, F2 & F3

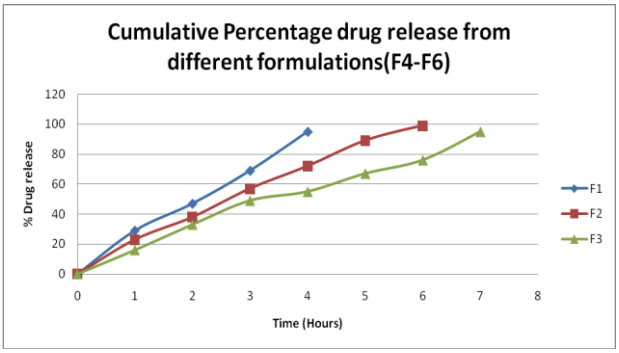

Fig 7:Cumulative % drug release of Moxifloxacin hydrochloride periodontal films formulations F4, F5 & F6

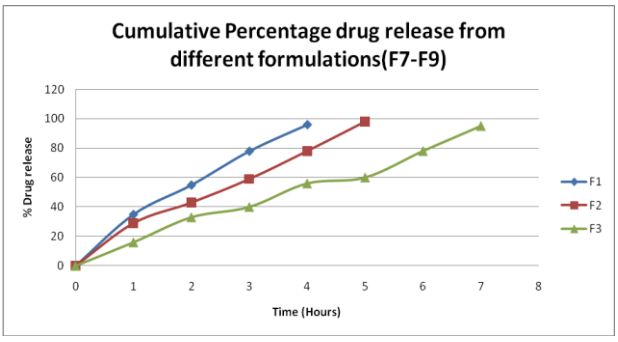

Fig 8: Cumulative % drug release of Moxifloxacin hydrochloride periodontal films formulations F7, F8 & F9

STABILITY STUDIES

Optimized medicated films were subjected to stability testing. Films were placed in a glass beaker lined with aluminium foil and kept in a humidity chamber maintained at 40 ± 2ºC and 75 ± 5% RH for 1 month. Changes in the appearance and drug content of the stored films were investigated after storage. The data presented were the mean of 3 determinations. Stability studies of the optimized formulation did not reveal any degradation of the drug and there was no significant change in the physical properties, drug content, and in vitro release profiles of the optimized formulation after storage for 3 months[30,31].

4. CONCLUSION

The study of present work is to extract Basil seed gum from basil seeds and Basil seed gum is used as novel excipient in the present study. To develop Periodontal films of Moxifloxacin hydrochloride by using polymers like Chitosan, Ethyl cellulose and Basal seed gum in different in different concentrations. The prepared films were evaluated for physicochemical properties, *in-vitro* drug release and antimicrobial activity. In most of the formulations with higher concentration range of polymers the percentage drug release was attained up to 85%. But according to drug release studies conducted by the higher concentration gave better drug release. Hence, the films with F6 and F9 formulations showed 95% drug release. Chitosan and Basil seed gum has shown equal drug release efficiency. Hence, it was concluded that basil seed gum can be used as novel polymer. Kinetic studies and accelerated stability tests were performed for optimized formulations F6 and F9. The formulations followed zero order release kinetics. Accelerated stability tests concluded that optimized formulation was stable and no physical changes were found.

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