Formulation and Evaluation of Moxifloxacin HCl from Topical Gel Preparations

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Abstract: Moxifloxacin HCl (moxi.HCl) is a fourth generation of fluoro-quinolone which has a broad spectrum and improved anti-bacterial activity over other similar quinolones. Topical gel formulations of moxi.HCl were prepared by using gel forming agents like Carbopol 934, methyl cellulose (MC), hydroxylpropylmethylcellulose (HPMC), sodium carboxymethylcellulose (Na CMC) and sodium alginate. Compatibility studies of the drug with these polymers were performed using DSC and FT-IR techniques. Physical characterizations of moxi.HCl gels including drug content, pH measurement and rheological parameter like viscosity were studied. In vitro drug release from the prepared gel and kinetics of release were evaluated. Microbiological studies of moxi.HCl gels were carried out by using agar plate method against the tested micro-organisms. Wound healing study was performed on wound of mice infected with S.aeurus and P.aeurginosa and treated with the prepared gels. Results revealed that all the used polymers in gel preparations are compatible with moxi.HCl. All the prepared gels followed non-Newtonian (shearing thinning) pseudo-plastic flow. Higher percent cumulative drug release (87.68±2.32%) was obtained from formula (F3) containing 0.1%w/w moxi.HCl and using 4% w/v HPMC as a gel base after 8 hrs. While, formula (F5) containing 0.1 %w/w moxi.HCl and using 6%w/v of sodium alginate as a gel base showed the lowest percent cumulative drug release (50.26±1.98%) after the same time. A slight decrease in the release rate of moxi.HCl was observed by increasing the concentration of the drug to 0.5%w/w in the prepared gels. The tested formulae (F1-F5) showed a higher antibacterial activity against S.aeurus and P. aeurginosa. Formula (F3) showed a higher % of wound healing reached to 100% reduction in wound area after 6 days of topical treatment to mice with S.aeurus infected wound. Hence from the overall study, it was concluded that moxi.HCl gel would be promising in the treatment of wounds.

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1. Introduction:

Moxi.HCl is a fourth generation fluoro-quinolone which has a broad spectrum anti-microbial effect against gram negative, gram positive micro-organisms and anaerobic bacteria. It is a DNA gyrase inhibitor, and also inhibits topoisomerase IV. DNA gyrase (topoisomerase II) is an essential bacterial enzyme that maintains the superhelical structure of DNA. DNA gyrase is required for DNA replication and transcription, DNA repair, recombination and transposition [(1)].

Moxi.HCl is a new 8-methoxyfluoroquinolone that has significant use in the treatment of bacterial infections of skin. It differs from the other quinolones by having a methoxy radical at the 8-position, an S, S-configured diazabicyclonoyl ring moiety at7-position and by having improved anti-bacterial activity over other similar quinolones [(2, 3, 4)].

Only moxi.HCl has regulatory approval for use in uncomplicated skin and skin structure infections (SSSIs) caused by S.aureus and S.pyogenes. It also received approval for use in complicated SSSIs caused by methicillin–susceptible S.aureus, E.coli, Klebsiella pneumoniae and Enterobacter cloacae [(5)]

Topical treatment with antibiotics has the advantages of avoiding the side effects caused by systemic treatment, avoiding difficulties associated with systemic application as poor tissue penetration in burned wounds and problems in blood vessels which carry systemic antibiotics to wound and decrease development of antibiotic drug resistance [(6)].

Applying topical gel to the skin and mucous membranes has the advantages of giving high rate of drugs release, rapid absorption, preventing entry of micro-organism into wound which leads to fast

healing of wounds and stable over long period of time [7].

Synthetic polymers e.g Carbopol 934 and semi-synthetic polymers e.g cellulose derivatives (MC, HPMC & CMC) are used to give the structural network, which is essential for the preparation of gels [8].

The objective of this work was to prepare topical gel of moxi.HCl to treat infected wounds and burns. Gel topical preparations were chosen to avoid the side effects of systemic preparation. Topical gel preparations containing moxi.HCl using different types and concentrations of gelling agents e.g.Carbopol 934, methylcellulose (MC), hydroxyl propylmethylcellulose (HPMC), sodium carboxy methy cellulose (NaCMC) and sodium alginate (Na. alginate) were prepared. Physical characterizations of the drug with the investigated polymers and in-vitro release of moxi.HCl from the prepared gels were also studied. Antibacterial activity and percent of wound healing were studied on wound of mice infected by the tested micro-organism.

2. Experimental:

Materials:

Moxi.HCl was obtained as a gift from Ranbaxy Laboratories, Gurgaon, India. Carbapol 934, methyl cellulose and hydroxypropyl-methyl cellulose were obtained from El-Gomhouria Co., Cairo, Egypt. Sodium carboxy methyl cellulose and sodium alginate were obtained from El-Nile Co., for pharmaceutical and chemical industry, Egypt. All chemicals used were of analytical grade and used as received.

Methods:

Compatibility studies:

Differential Scanning Calorimetry (DSC) Studies:

Thermal characterization of pure drug, the used polymer alone and their physical mixtures (1:1 w/w) was performed using Differential Scanning Calorimeter (DSC-50, Shimadzu, Japan.). Samples were placed in sealed aluminum pans. The samples were scanned at 20ºC /min. starting from 20ºC to 300ºC.

FT-IR studies:

The drug-excipient compatibility study was determined by Fourier Transform Infrared Spectroscopy(FT-IR), Nicolet 6700FT-IR,Thermo Fisher, Madison, USA, using KBr pellets of 0.1mm.The IR spectra of the drug alone, the used polymer gel bases alone and their physical mixtures (1:1 w/w) were determined to predict any interaction between the drug and the used polymer.

Preparation of moxi.HCl gels:

The composition of the formulated gels of moxi.HCl is illustrated in Table (1).The required amount of drug is dissolved in 50 ml purified water using magnetic stirrer, then the required weight of each polymer was added slowly with continuous stirring until transparent gels were formed. Care was taken that no lamps of polymer were formed during stirring. Carbopol934 was sprinkled over water and allowed to hydrate overnight. The solution was again stirred with magnetic stirrer after 24 hours. Triethanolamine was then added to neutralize pH of the mixture.

Table (1): Composition of the formulated gels of moxi.HCl.

	Weights of drug and excipients in each formula (%w/v)									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Moxi.HCl	0.1	0.1	0.1	0.1	0.1	0.5	0.5	0.5	0.5	0.5
Carbopol 934	0.5					0.5				
MC		8					8			
HPMC			4					4		
NaCMC				7					7	
Sod.alginate					6					6
Propyl paraben	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
Propylen glycol	10	10	10	10	10	10	10	10	10	10
Triethanolamine	1					1				
Water to…ml	100	100	100	100	100	100	100	100	100	100

Organoleptic properties:

The appearance was checked visually for the color, homogeneity and transparency. They were tested for their appearance and presence of any aggregates [8].

Drug content:

The drug content was determined by taking 1 ml sample of each gel into 100 ml volumetric flask and diluting with 100 ml of buffer solution of pH 7.4. Serial dilution from this solution was done by taking 1 ml of sample and diluted again by 10 ml of buffer solution of pH 7.4. The absorbance of the drug was

measured at 289 nm by UV-Spectrophotometer (UV-Visible Spectrophotometer, Jenway-model 6305, England) and calculate the percentage of drug content in gel preparation.

Measurement of pH:

The pH of gel formulae was measured using pH meter (Digital pH meter, Jenway-model 3310, England), the test was done in triplicates.

Rheological studies:

The rheological behaviors of the prepared formulae were determined using Brookfield Viscometer (DV.III Ultra Programmable Rheometer), using spindle number 96 at temperature 28.8ºC.The spindle was kept to rotate for one minute before measuring the shear stress and viscosity. The viscosity of the formulation was determined at different speed conditions 2, 4, 6, 8 and 10 rpm. The test was done in triplicates.

In vitro release of moxi.HCl gels:

In vitro release studies of moxi.HCl gels were performed using modified USP dissolution apparatus I [(9&10)]. Glass cylinder opened from the two sides. These cylinder were fixed on each paddle by rubber thread, one end is closed by cellophane membrane. The other end left opened. The cellophane membrane can allow the release of the gel through it. It must be soaked in buffer solution over night before the test. It was tied well to the end of cylinder. The cylinder has diameter of 2.5cm and surface area of 4.9cm^2.Accurate weight of 1.5 gm of the prepared gel was placed on the cellophane membrane inside the cylinder. The dissolution medium is 200 ml of buffer pH 7.4 thermostat at 37ºC. The paddles were rotated at 50 rpm. Samples (2ml) were withdrawn at time interval up eight hours. The volume of each withdrawn sample was replaced by the same volume of buffer solution maintained at the same temperature to keep constant volume. The drug content was analyzed using UV-Spectrophotometer at 289 nm.

Release kinetics:

In order to understand the mechanism and kinetics of drug release, the results of in vitro drug release study were fitted to various kinetics equations like zero order, first order and Higuchi model. In order to define a model which will represent a better fit for formulation, drug release data were further analyzed by Peppas equation, $\mathbf{M_t/M_\infty = kt^n}$, where $\mathbf{M_t}$ is the amount of drug released at time **t** and $\mathbf{M_\infty}$ is the amount released at $\mathbf{t_\infty}$, $\mathbf{M_t/M_\infty}$ is the fraction of drug released at time t,**k** is the kinetic constant and **n** is the diffusional exponent, a measure of the primary mechanism of drug release $\mathbf{r^2}$values were calculated for the linear curves obtained by regression analysis of above plots.

Antimicrobial studies:

The antibacterial activity of moxi.HCl gels against different types of micro-organisms (S.aeurus, E.coli, MERSA, K.pneumoniae and P.aeurginosa) was studied. A layer of nutrient agar (20ml) seeded with the test micro-organisms (0.2 ml) was allowed to solidify in the Petri plate. Pores were made in the solidified agar layer with the help of sterile borer at 4mm diameter. Then accurate amount of the prepared gels were taken by syringe poured in each pore. The plates were incubated for 24 hours at 37ºC.The zone of inhibition was measured and each sample was tested in triplicates [(11)].

Wound healing studies

Induction of infected wounds:

The animal study was conducted following approval of protocols by Institutional Animal Ethics Committee (I.A.E.C). Male albino mice, pathogen free, 25 ± 5 gm were obtained. General anesthesia was performed using pentobarbital (50 mg/kg, IP). The hair was shaved and skin was sterilized with 80% ethyl alcohol. A full thickness wound was created using a BO-chamber round scalpel and no. 11 blade followed by division of the mice into five groups. First group had been inoculated with 1×10^8 CFU/ml S.aeurus colony. Second and fourth groups were inoculated with 1×10^8 CFU of P.aeurginosa.The third and the fifth groups were inoculated with S.aeurus.

Assessment of infected wound healing

The groups were distributed as follows: Group 1 and 2 were considered as control, excision wound of mice infected with S.aeurus and P.aeurginosa respectively without treatment. Group 3 and 4 excision wound of mice infected with staph and P.aeurginosa respectively and treated with moxi.HCl gel. Group 5 excision wound of mice infected with S.aeurus and treated with moxi.HCl orally through stomach tube. After the first treatment, the mice were placed in individual cages in a temperature-controlled room (22°C) with food and water provided ad libitum and a 12-h/12-h dark/light cycle. Bacterial swabs and imaging of the wound were carried out at days 0, 2, 4, 6, 8, and 10. Wound contraction was monitored by measuring wound area plan metrically. Results underwent statistical analysis of variance and independent t- tests when data were normally distributed (SPSS, Chicago, IL).

3. Results and Discussion:

Differential Scanning Calorimetry (DSC) Studies:

Figs. (1-3) showed the DSC thermograms of moxi.HCl alone, polymer alone and their physical mixtures (1:1 w/w). Moxi.HCl showed endothermic peak at 258ºC which corresponding to its melting and followed by exothermic peak at 263ºC due to its decomposition. The physical mixtures of moxi.HCl

with each polymer showed the same endothermic peak of the drug at 258° C with a decrease in their intensity that may be attributed to the dilution effect. Minor decrease in melting point of the drug with sodium alginate was observed. The obtained results revealed that there is no interaction between the drug and the used polymers. These results will be confirmed by FT-IR studies.

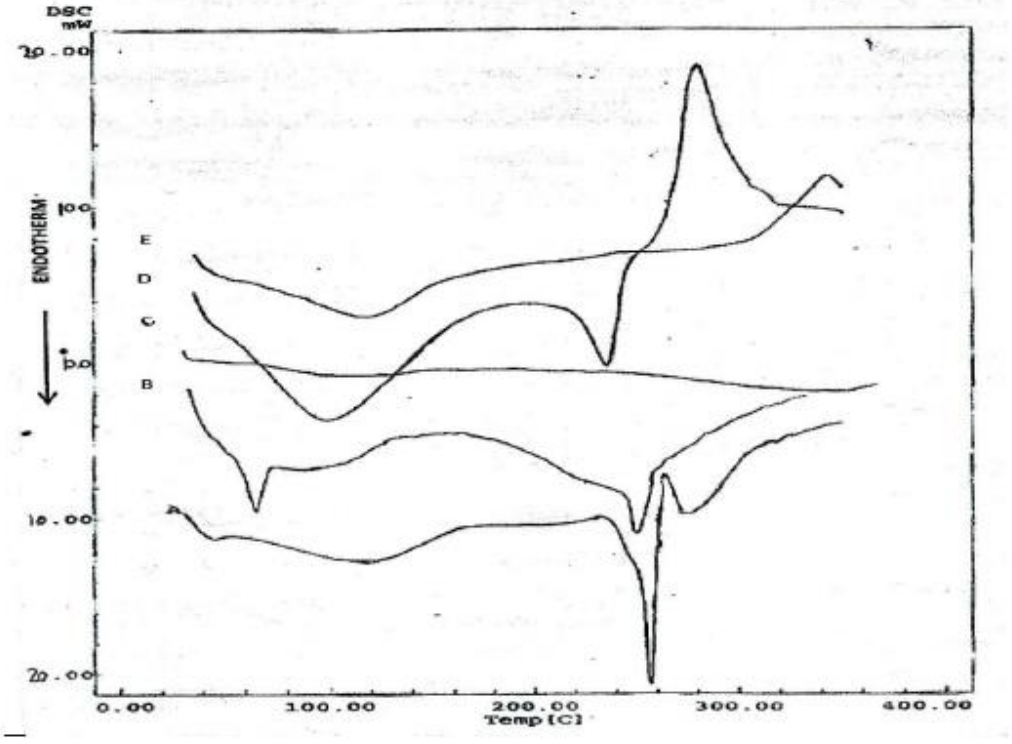

Fig (1): DSC thermograms of moxi.HCl alone, polymer alone and their physical mixtures (%w/w);(A) Moxi.HCl alone,(B) Moxi.HCl with carbopol 934,(C) Carbopol 934 alone, (D)Moxi.HCl with Na CMC&(E) Na CMC alone.

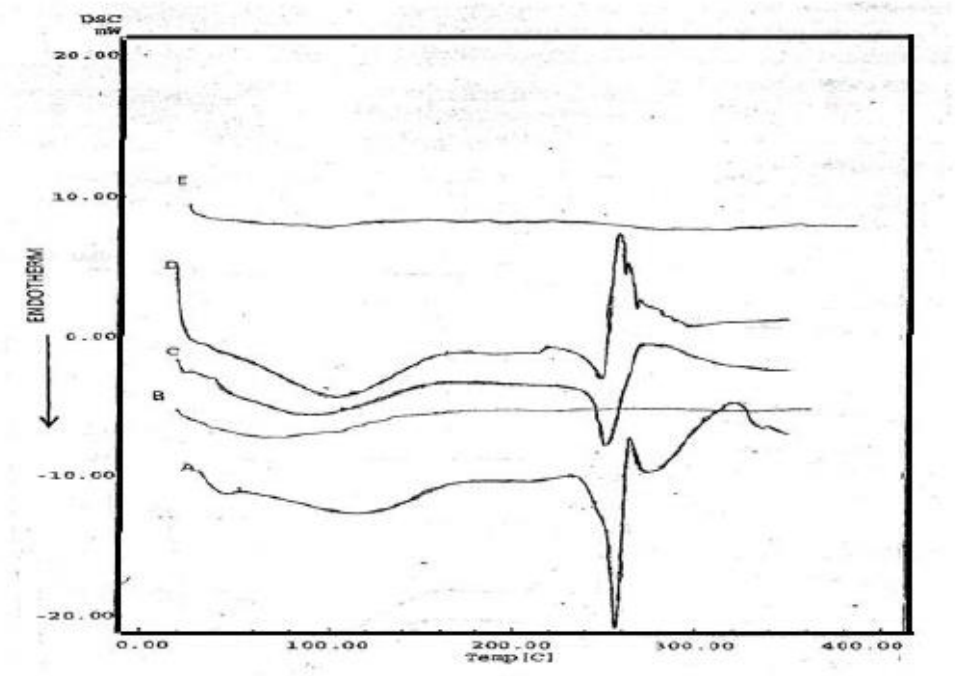

Fig (2): DSC thermograms of moxi.HCl alone, polymer alone and their physical mixtures (1:1w/w);
(A) Moxi.HCl alone,(B) MC alone, (C) Moxi.HCl with MC,(D) MoxiHCl with HPMC&(E) HPMC alone.

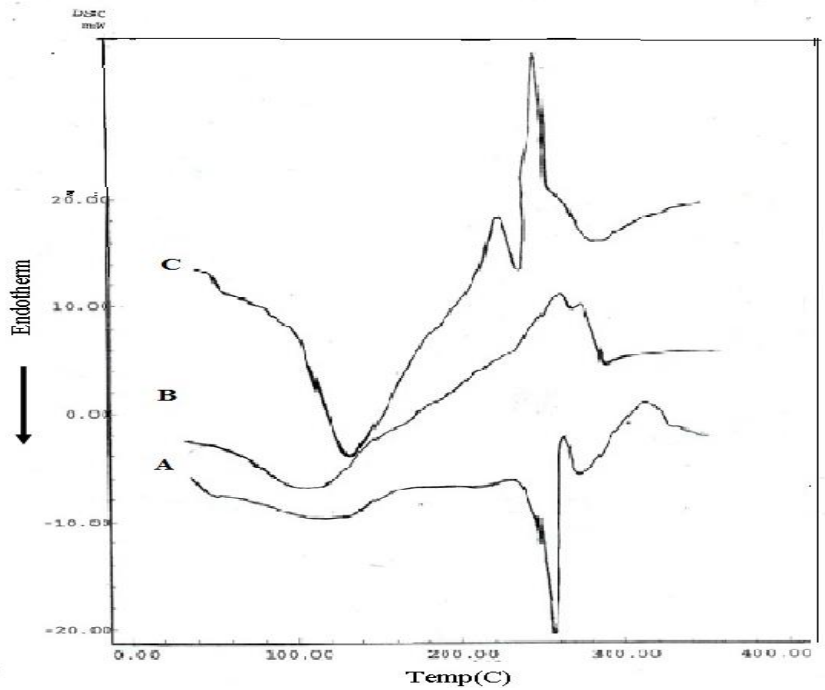

Fig (3): DSC thermograms of moxi.HCl alone, polymer alone and their physical mixtures (1:1w/w); (A) Moxi.HCl alone, (B) Na.alginate alone & (C) Moxi.HCl with Na alginate.

Fourier Transform Infrared (FT-IR) Studies

The FT-IR spectra of pure moxi.HCl, polymer alone and their physical mixtures of the drug with the used polymers (1:1 w/w) are shown in Fig. (4). The spectra obtained from FT-IR studies ranged from wave length of 4000 cm^{-1} to 400 cm^{-1}. FT-IR of moxi.HCl showed characteristic peaks at 1697 cm^{-1} due to carboxylic acid C=O stretching, C-N stretching at 1342 cm^{-1}, aromatic C=C stretching at 1612 cm^{-1}, 1506 cm-1 and 1444 cm-1. From the spectral study, it was observed that there is no shifting in wave length of drug peaks in its physical mixtures with the used polymers. This indicated that there is no interaction between the drug and the used polymer in formulae.

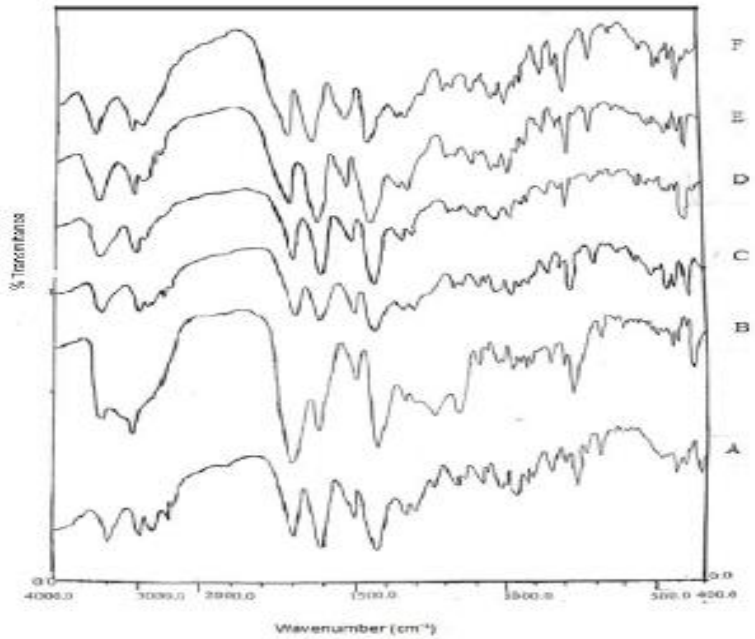

Fig (4): FT-IR spectra of moxi.HCl alone and their physical mixtures (1:1w/w); (A) Moxi.HCl alone,(B) Moxi.HCl with Carbopol, (C) Moxi.HCl with MC, (D) Moxi.HCl with HPMC, (E) Moxi.HClwith NaCMC&(F) Moxi.HCl with sod.alginate.

Organoleptic properties, drug content and pH-measurement:

Table (2) illustrated that all the formulae are light yellow in color. While, yellowish brown color with Na alginate was observed. Most of formulae are transparent. The pH of formulae was found to be in the range of 6.1 ± 0.78 to7.4 ± 0.34. The drug content was in the range of 93.88 ± 0.45 to 98.56 ± 0.76 %, Table (2).

Table (2): Organoleptic properties, drug content and the pH of the prepared gels.

Formula No.	Color	Transparency	Drug content%	pH of gel
F1	Light yellow	Transparent	96.4±0.7	7.4±0.34
F2	Light yellow	Transparent	98.6±0.67	7.2±0.46
F3	Light yellow	Transparent	95.7±0.86	6.4±051
F4	Light yellow	Transparent	97.6±1.08	6.7±0.48
F5	Yellowish brown	Translucent	93.9±0.45	6.1±0.78
F6	Light yellow	Transparent	97.3±0.63	7.8±0.39
F7	Light yellow	Transparent	96.5±0.65	6.3±0.65
F8	Light yellow	Transparent	98.6±0.76	6.8±0.87
F9	Light yellow	Transparent	92±0.68	6.3±0.69
F10	Yellowish brown	Translucent	94.85±1.2	6.2±0.93

Rheological studies:

All formulae showed pseudo-plastic behaviors which indicated by that the increase in shear rate, the viscosities of the formulae were decreased, Figs. (5-7). All the prepared gels showed non-Newtonian (shearing thinning) pseudo-plastic flow, Figs. (8-10).

In vitro release of moxi.HCl gels:

Figs. (11&12) showed the release profiles of different concentrations of moxi.HCl (0.1% and 0.5%) from the prepared gels using different types of polymers as a gelling agent in pH 7.4 for 8 hrs. The used polymers are namely; HPMC, MC, Carbopol 934, Na CMC and Na alginate.

The release of the drug from these gels was characterized by initial phase of high release (burst effect) and as the gelation proceeded, the remaining drug was released at a slower rate (second phase). This bi-phasic pattern of release is characteristic feature of matrix diffusion kinetics.

The percent released of moxi.HCl (0.1% w/v, F1-F5) from the prepared gels are ranged from 50.26 ± 1.98% to 87.68 ± 2.32%. The release of the drug from the prepared gels decreased in the following order: HPMC > Carbopol 934> MC > NaCMC> Na alginate as shown in Fig. (11).

Formula (F3) containing 0.1% of moxi.HCl using HPMC as a gelling agent showed the maximum percentage release of the drug which reached to 87.68 ± 2.32 % after 7 hrs. While the lowest percentage release of the drug was 50.26 ± 1.98% which obtained from formula (F5) containing 0.1% w/w moxi.HCl using Na alginate as a gelling agent.

Fig (12) showed the release of moxi.HCl (0.5% w/v) from different types of polymers as gelling agents (F6-F10) at pH 7.4 for 8hrs. The release of drug from these polymer are decreasing in the following manner; Carbopole 934 > MC > HPMC > Na alginate > NaCMC. The maximum percentage release of moxi.HCl from Carbopol 934 was 78.14 ± 3.43 % after 8hrs. The enhanced drug release from Carbopol gel base may be attributed to the presence of pores in the gel which allow relatively free release of the drug to the vehicle and lack of over solubilization of the lipophilic drug in aqueous vehicle and hence readily be available for release [(11)]. While the lowest % release of drug 52.52 ± 1.3% from the gel using NaCMC (F9) was observed, Fig. (12). The higher release of the drug from gels using MC (F7) and HPMC (F8) than that from Na.CMC (F9) may be attributed to the higher solubility of moxi.HCl in NaCMC, in addition to the higher viscosity of NaCMC [(12)]. The release profile of moxi.HCl gels showed bi-phasic release pattern which beneficial in terms of antibacterial activity to achieve therapeutic concentration of drug in minimal time followed by constant release to maintain sustained and controlled release of the drug [(13)]. Minor decrease in release rate of moxi.HCl from the prepared gel on increasing the concentration of the drug from 0.1% to 0.5%w/w was observed, Fig. (12).

Release kinetics:

In vitro release profiles were fitted to various kinetic models in order to find out the mechanism of drug diffusion. The rate constant was calculated from the slope of the respective plots. The various kinetic equations, zero order, first order and Higuchi model are shown in Table (3). It is clear, that the release of moxi.HCl from the prepared gels using MC (F2) and HPMC (F3) are best fitted to simplified Higuchi model as indicated from highest regression coefficient (r^2). While the release of moxi.HCl from the prepared gels using Carbopol 934 (F1), NaCMC (F4) and Na.alginate (F5) are followed zero order release that

may attributed to the high viscosity of the prepared gel. This release behavior developed a sustained release drug delivery system where the release of drug occurs in a constant rate for extended period of time.

To understand the mechanism of release of moxi.HCl from the prepared gel the release data were analyzed using the equation proposed by Peppas [14]. $M_t/M_\infty = kt^n$. The results of these fitting are presented in Table (4) and showed that the values of **n** (release exponent) of all formulations lie between 0.45 and 0.89 indicating that the drug release is non-Fickian i.e., the mechanism of the drug release is due to polymer relaxation as well as diffusion and erosion.

Antimicrobial studies:

The antibacterial activity of moxi.HCl gels against the tested micro-orgnisms was evaluated by measuring the diameter of the zone of inhibition as shown in, Table (5) and Fig. (13).

Also, formula (F3) which gave a higher release of the drug and good rheological behavior was chosen for further antimicrobial activity and wound healing in vivo. The inhibition zone of formula (F3) against MERSA, K. pneumonia and P. aeurginosa were 30± 1.4 mm, 13±1.56 mm and 40± 1.45 mm respectively.

These results indicated the efficiency of the prepared gels of moxi.HCl against all the tested micro-organisms.

Wound healing

Wound contraction mainly depends on the repairing ability of tissue, which may be reduced due to infection. Figs. (14-17) showed the macroscopic photographs for mice with S.aeurus infected wounds before and after treatment with moxi.HCl gel (F3). Topical application of moxi.HCl gel (F3) to mice with S.aeurus infected wounds gave 40% wound contraction within 2nd days. There was a higher significant value of % healing of wounds ($P< 0.05$) for topical application of (F3) over the control mice which showing 25% wound contraction within the same day. Rapid healing of wounds in mice treated with moxi.HCl gel was illustrated by 40%, 44%, 70% and 100% of wound contraction at 2,4,6 and 8 days respectively. Also rapid reduction in bacterial count to 0% after 6 days of treatment of mice with S.aeurus infected mice was observed. Topical application of moxi.HCl gel to mice with S.aeurus infected wound showed higher % of wound contraction (reached to 70) than that orally administration of the drug to infected mice (reached to 52%) within 6 days of treatment. Rapid healing of wounds was observed for mice with S.aeurus infected wound than that with P. aeurginosa.

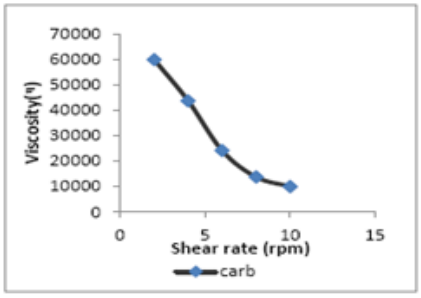

Fig.(5): Viscosity study of gel using Carbopol (F1) in cps as a gelling agent.

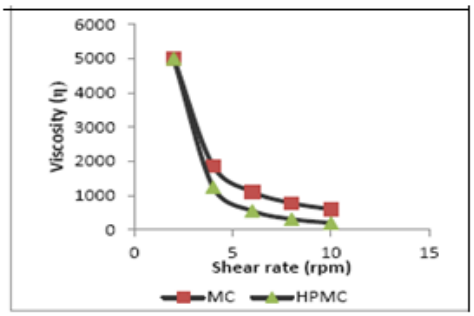

Fig.(6) Viscosity study of MC (F2) and HP (F3) in cps as gelling agents.

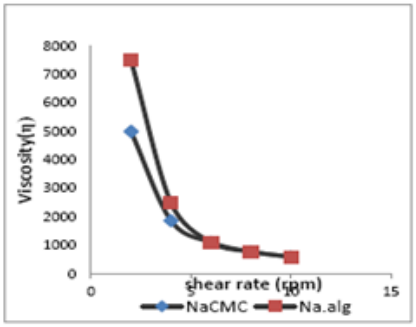

Fig. (7) Viscosity study of NaCMC gel (F4) and Na.alginate (F5) in cps as gelling agents

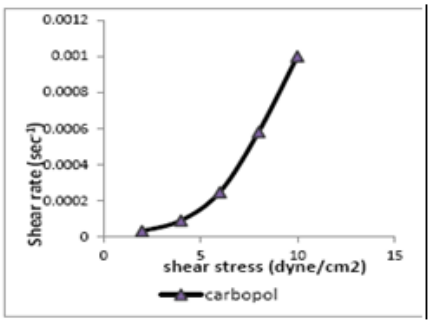

Fig.(8): Rheological behavior of Carbopol 934 gel (F1).

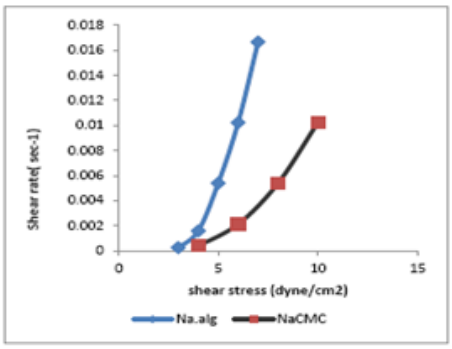

Fig (9): Rheological behaviors of NaCMC gel (F4) and Na.alginate gel (F5).

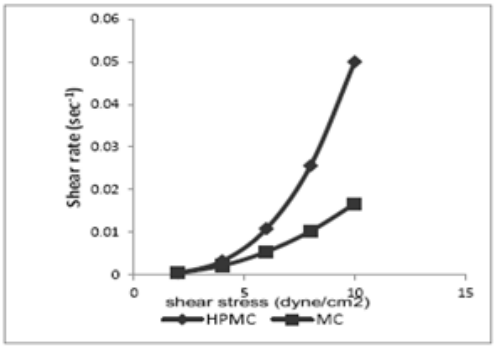

Fig (10): Rheological behaviors of MC (F2) and HPMC gel (F3)

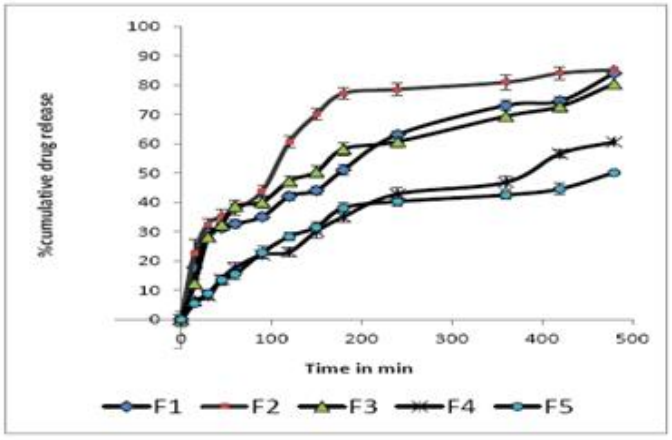

Fig (11) : Release profiles of moxi. HCl from gels prepared using different polymers .

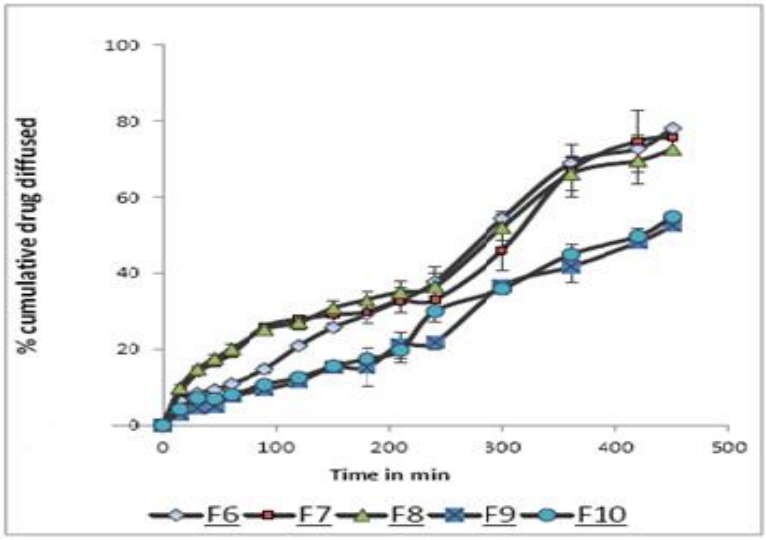

Fig (12): Release profiles of moxi. HCl from gels prepared using different polymers.

Table (3): Release kinetics of moxi.HCl from the prepared gels (F1:F10) at pH 7.4.

Formulae No	Correlation coefficient (r^2)			Mechanism of release	K-value
	Zero order	First order	Higuchi model		
F1	0.97932	-0.99026	0.985532	Higuchi model	3.46
F2	0.967888	-0.97639	0.978552	Higuchi model	5.32
F3	0.919784	-0.96906	0.973809	Higuchi model	3.51
F4	0.980141	-0.99054	0.995993	Higuchi model	3.08
F5	0.949715	-0.96196	0.98515	Higuchi model	2.96
F6	0.988142	-0.97338	0.963879	Zero order	0.141
F7	0.957778	-0.95552	0.966623	Higuchi model	2.403
F8	0.953504	-0.966	0.985034	Higuchi model	2.00
F9	0.960695	-0.94175	0.924589	Zero order	0.095
F10	0.977988	-0.96535	0.946195	Zero order	0.087

Table (4):Kinetic analysis of the release data of moxi.HCl gels.

Formula No.	**n**	**K**	**r^2**
F1	0.528	0.679	0.993
F2	0.458	5.017	0.963
F3	0.488	4.713	0.983
F4	0.799	0.451	0.996
F5	0.635	1.145	0.981
F6	0.769	0.598	0.972
F7	0.595	1.725	0.964
F8	0.535	2.289	0.955
F9	0.851	0.2357	0.977
F10	0.744	0.7449	0.964

Table (5):Antibacterial activity of moxi.HCl gels.

Type of micro-Organism	Diameter of the zone of inhibition in (mm)				
	F1	F2	F3	F4	F5
S.aeurus	47±1.2	46±1.09	47±1.6	44±1.02	47±1.7
E.coli	18±0.9	19±1.5	18±1.45	17±0.8	16±1.3

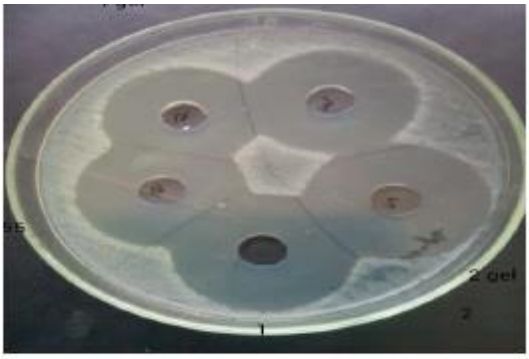

Fig. (13) Inhibition zone of moxi.HCl gels aganist *S.aeurus*.

Fig.(14) Control mice wound infected with *S.aeurus*.

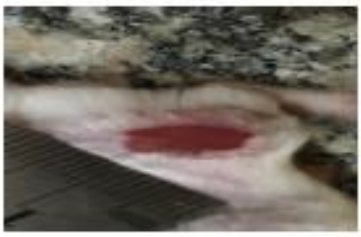

Fig.(15) Control mice wound infected with *S.aeurus* after 2days without treatment

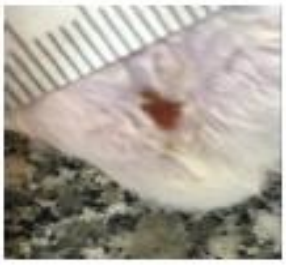

Fig.(16) Mice wound infected with *S.aureus* after 2days of treatment by moxi.HCl gel.

Fig. (17) Mice wound infected with *S.aureus* after 6 days of treatment by moxi.HCl gel

Conclusion:

From the obtained results, it can be concluded that moxi.HCl gels were prepared successfully using Carbopol 934, MC, HPMC, Na CMC and Na alginate. The gels prepared showed a non-Newtonian behavior and have pH suitable for topical application. There is no interaction between the drug and the used polymers in the preparation of moxi.HCl gels as illustrated by DSC and FT-IR studies. In vitro release showed good release from the formulae prepared by Carbopol 934, MC and HPMC. Microbiological studies showed excellent antimicrobial activity against S.aeurus, P.aeurginosa and MERSA which considered the main cause of infected wounds and burns. Also have a good and acceptable activity against E. coli and K.pneumonia. These results demonstrated the effective use of moxi.HCl gels as topical gel for treatment of infected wounds and burns. It was observed that the topical gel of moxi.HCl used in wound healing can provide a new choice of topical delivery system for the effective management of wound infections.

References:

1. The Merck Index, Merck Research Laboratories, white house Station, New Jersey, USA, 14, 1087, (2006).
2. Siefert H.M., Domdey-Bette A, Henninger K., Hucke F., KohlsdoferC, Stass H H. (Pharmacokinetics ofthe 8-methoxyquinolone, moxifloxacin a coparison in humans and mammalian species). J Anti microb Chemother 43 (suppl B): 69-76 (1999May).
3. Stass H.H.,Dalhoff A., Kubitza D. and Schuhly U. (Pharmacokinetics, safety and tolerability of ascending single doses of moxifloxacin. a new 8-metothoxyquinolone administered to healthy subjects). Antimicrob agents Chemother 42 (8):2060-5 (1998).
4. Malathum K.,singh K.V. and Murray B.E. (In vitroactivity of moxifloxacin, a new 8-metothoxyquinolone against Gram-positive bacteria). Diagn Microbial Infect Dis 35 (2): 127-133 (1999).

5. Abdellaziz L.M. and Mervat M.Hosny M. M. (Development and validation of Spectrophotometric, atomic absorption and kinetic methods for determination of moxifloxacin hydrochloride).Analytical Chemistry Insights; 6, p67 (2011).
6. Jacobsen F., Fisahn C, Sorkin M, Thiele I,Hirsch T, Stricker I, Klaassen T, Roemer A, Fugmann B, and Steinstraesser L. (Efficacy of topically delivered moxifloxacin against wound infection by Pseudomonas aeruginosa and methicillin – resistant Staphylococcus aureus).Antimicrobial Agents and Chemotherapy;p2325-2334 (May 2011).
7. Langley C.A. and Belcher D. (Pharmaceutical Compounding and Dispensing). Puplushied by Pharmaceutical press p107, (2008).
8. Kaur L. P. and Guleri T.K (Topical gel: a recent approach for novel drug delivery). Asian.J.Bio.Pharm.Sci. (2013).
9. Ueda C.T, Shah V. P.,Derdzinski K., Ewing G., Flynn G., Maibach H., Marques M, Rytting H, Shaw S, Thakker K and Yacobi A. (Topical and transdermal drug products) Pharmacopeial forum, Vol.35(3) P.750May-June (2009).
10. Mudgil M. and Pawar P. K. (preparation and In vitro Evaluation of Moxifloxacin-loaded PLGA nanosuspentions of ophthalmic application) Sci.Pharm;81(2),591-606 (2013).
11. Dhavse V.V. and Amin. P.D. (Formulation and evaluation of topical bases of ketoprofen). East Pharm. 133-135 (1997).
12. Al-KhashabY.E.N., Al-Mulla Hummadi Y.M.K,Hamadi S.A.,and Al-waizM. M. (Formulation and evalution of ciprofloxacin as topical gel).AJPS, Vol.8, No,2 (2010).
13. Sabitha K., Sajeeth C. I. and Santhi K. Chitosan nanoparticles: A novel vehicle for the enhanced ocular delivery ofMoxifloxacin HCl. Research Journal of Pharmaceutical, Biological and Chemical Sciences. Vol. 3 issue 2 p.534. June (2012).
14. Ritger P.L. and Peppas N.A. (A simple equation for description of solute release II Fickian and anomalous release from swellable devices). J.control release. 5(1), 37-42, 1987.

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