International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 9, Issue 3, 2017

Original Article

DEVELOPMENT AND PHYSICAL CHARACTERIZATION OF A PERIODONTAL BIOADHESIVE GEL OF GATIFLOXACIN

HANAN JALAL KASSAB*, LENA MURAD THOMAS, SABA ABDULHADI JABIR

Department of Pharmaceutics, College of Pharmacy, University of Baghdad, Iraq-Baghdad
Email: hanan70k@gmail.com

Received: 12 Jan 2017, Revised and Accepted: 17 Apr 2017

ABSTRACT

Objective: The aim of this study was to develop a bioadhesive gel of gatifloxacin for the treatment of periodontal diseases.

Methods: Periodontal gels of gatifloxacin were prepared using different hydrophilic polymers such as carbopol 940 (CP 940), carboxymethyl cellulose (CMC) and hydroxypropylmethyl cellulose (HPMC) in varied concentrations, either alone or as a combination. The prepared gels were evaluated for their physical appearance, pH, drug content, viscosity, bioadhesiveness and *in vitro* drug release profile. The influence of the type and the concentration of polymer on the drug release as well as on viscosity and mucoadhesiveness of prepared gels were investigated.

Results: The prepared gels showed acceptable physical properties concerning color, homogeneity, consistency, spreadability, and pH value. Using different polymer types at different concentrations, as well as different polymer combinations, play a significant role in the variation of overall characteristics of formulations. Increasing the concentration of polymer increased the viscosity as well as mucoadhesion, and reduced drug release rate. Formulation F 11 (1 % CP 940 and 5 % CMC) was selected as the formula of choice based on the data of various evaluation parameters such as pH, drug content, viscosity, spreadability and bioadhesion as well as its ability to show a prolonged drug release pattern.

Conclusion: The obtained results show that a bioadhesive periodontal gel of gatifloxacin can be prepared using hydrophilic polymers, and by using a combination of polymers the viscosity, mucoadhesiveness, spreadability and release behavior can be optimized.

Keywords: Gatifloxacin, Mucoadhesive, Periodontal gel

DOI: http://dx.doi.org/10.22159/ijap.2017v9i3.17056

INTRODUCTION

Periodontal disease is an infectious condition caused by bacterial accumulation that involves gingiva but can also spread to deeper supporting tissues of the teeth, leading to inflammation and degeneration of the gingiva and tooth loosening and eventually teeth loss when left untreated [1]. Several approaches to treat periodontitis range from mechanical debridement of tooth surfaces to systemic or local administration of antimicrobial agents [2, 3]. Because of significant side effects associated with the systemic administration of antibiotics, this approach of treatment should only be used in patients who respond poorly to mechanical treatment [4].

Local antimicrobial delivery system in periodontal pockets overcome limitations caused by systemic drug administration and has the benefit of maintaining adequate concentration of drugs at the target site. It have been carried out using a variety of approaches including oral rinses, sub-gingival irrigation and antimicrobial agents controlled release delivery systems such as fibers, films, chips, gels, ointments, and micro-particles which have been seen to be effective methods to administer antimicrobial agents in periodontal therapy [5, 6].

Gatifloxacin (GT) is a fourth generation fluoroquinolone, with a broad antibacterial spectrum, including a number of aerobic, anaerobic, gram positive bacteria, is was shown to be highly active against penicillin sensitive and resistant Streptococcus pneumoniae, Staphylococcus aureus, Streptococcus pyogenes and Streptococcus agalactiae and a number of gram-negative microorganisms [7]. The aim of the present study was to formulate bioadhesive periodontal gels of gatifloxacin with appropriate viscosity, spread ability, and release behavior so as to provide localized and prolonged drug release for better management of local periodontal infections.

MATERIALS AND METHODS

Materials

Gatifloxacin (gift from Kanawati pharmaceutical company, Syria), carbopol 940 (CP940), hydroxyl propyl methyl cellulose (HPMC) (Himedia, India), carboxy methyl cellulose (CMC) (supplied by Samarra Drug industries, Iraq), agar (Himedia, India), triethanolamine (TEA) (Hopkins and Williams Ltd., England), citric acid, disodium hydrogen phosphate, mannitol, methylparaben (MP) and propyl paraben (PP) (Gainland Chemical Co. Ltd., UK). All chemicals used were of analytical grade.

Methods

Preparation of gatifloxacin periodontal gels

Gatifloxacin (GT) periodontal gels were prepared using Varshosaz *et al.* method [8]. To prepare the gels, weighed amounts of the polymers (CP 940, CMC, or HPMC) was dissolved in 75 ml of McIlvaine buffer (pH 6.6) using a magnetic stirring bar. Gatifloxacin (0.5 % w/v) was dissolved in small volume of 0.1 N HCl solution, then the drug solution was added to the polymeric solution with stirring. Mannitol, and preservatives (methyl and propyl paraben) were added with continuous stirring to the formulation and volume was then brought up to 100 ml using McIlvaine buffer (pH 6.6).

The pH of gels containing CP 940 was adjusted to pH 6.8 using triethanolamine. The prepared gel formulations were stored in suitable wide mouth plastic jars with a screw capped lids at room temperature until required. Table 1 shows the composition of all the formulations.

Evaluation of gatifloxacin periodontal gels

Physical appearance of gel formulations

All prepared formulations were visually inspected for their color, consistency, homogeneity, presence of aggregates, grittiness and phase separation after the gels have been set in the container [9].

pH determination

The measurement of formulations pH was done using a digital pH meter (CG 820, Schott Geräte GmbH, Hofheim, Germany) by dipping the electrode completely into the gel so as to cover the electrode. Obtained values were the average of three readings [10].

Estimation of drug content

Accurately weighed amount of formula (1 g) equivalent to 5 mg of gatifloxacin was taken in a 100 ml of McIlvaine buffer (pH 6.6) in volumetric flask. The volumetric flask was sonicated to get complete solubility of the drug, and then kept overnight for complete dissolution. After filtration through 0.45µm membrane filter, 1 ml of the solution was diluted to 10 ml with McIlvaine buffer (pH 6.6) and drug absorbance of sample solution was determined against McIlvaine buffer (pH 6.6) as a blank and at λ max 286 nm using Biotech 9200 UV Vis spectrophotometer.

The drug content was calculated from the linear regression equation obtained from the calibration data [11].

Table 1: Compositions of gatifloxacin periodontal gel formulations

	Ingredients (% w/v)							
Code	**Drug**	**CP 940**	**CMC**	**HPMC**	**Mannitol**	**MP**	**PP**	**McIlvaine buffer (pH 6.6, up to)***
F1	0.5	0.75	-------	-------	1	0.18	0.02	100 ml
F 2	0.5	1.0	-------	-------	1	0.18	0.02	100 ml
F 3	0.5	1.5	-------	-------	1	0.18	0.02	100 ml
F 4	0.5	-------	3	-------	1	0.18	0.02	100 ml
F 5	0.5	-------	5	-------	1	0.18	0.02	100 ml
F 6	0.5	-------	7	-------	1	0.18	0.02	100 ml
F 7	0.5	-------	-------	5	1	0.18	0.02	100 ml
F 8	0.5	-------	-------	10	1	0.18	0.02	100 ml
F 9	0.5	-------	-------	15	1	0.18	0.02	100 ml
F 10	0.5	1.0	3	-------	1	0.18	0.02	100 ml
F 11	0.5	1.0	5	-------	1	0.18	0.02	100 ml
F 12	0.5	1.0	-------	5	1	0.18	0.02	100 ml
F 13	0.5	1.0	-------	10	1	0.18	0.02	100 ml
F 14	0.5	-------	3	5	1	0.18	0.02	100 ml
F 15	0.5	-------	3	10	1	0.18	0.02	100 ml

*Carbopol containing formulations were adjusted to pH 6.8, CP 940 = carbopol 940, CMC = carboxymethyl cellulose, HPMC =hydroxypropyl methylcellulose, MP = methyl paraben, PP = propyl paraben

Viscosity study

Viscosity of formulations was studied using Myr VR 3000 digital viscometer. Viscosity of the samples was measured at 25◦ C using 100 ml aliquots. Measurements were made at 100 rpm using a suitable spindle number depending on the sample viscosity. The average of three readings was used to calculate the viscosity and obtained values were recorded as milliPascals per second (mPa. s) [12].

Spreadability

The spreadability of formulations was determined 48 h after preparation by parallel plate method [13]. A sample (1g) of the formulation was transferred to the center of glass plate (20 x 20 cm) placed over a paper on which concentrically divided squares of 1 mm sides were drawn, and spread over an area of 1 cm^2. Another glass plate having a mass of 100 g was placed gently on the formulation, and 2 kg weight was placed at the center of the plate with care to avoid sliding of the glass plate. The spread diameter in cm was measured after 3 min where no more spreading was expected. Results obtained are the average of three determinations [14].

Bioadhesion study

Adhesiveness of formulations was measured by the plate agar method. An agar plate (containing 2% w/v agar) of 5 cm in diameter was prepared; 1 g of the formulation was placed on the center of the agar plate, making a circle of 1 cm in diameter. The plate was slanted at 30 ° for 1 hour and the longest distance moved by the sample was measured at room temperature [15].

***In vitro* drug release study**

In vitro drug release study was carried out using RC-6 dissolution tester. One gram of the formulation was weighed on an analytical balance and spread evenly on the surface of a watch glass, then was gently lowered through 500 ml of the dissolution medium (McIlvaine buffer; pH 6.6). The paddle of the dissolution apparatus was centrally positioned 2.5 cm above the watch glass. The release study was carried out at 37±0.5 ◦C and the paddles were rotated at a stirring rate of 50 rpm. Aliquots of 5 ml were withdrawn at specified time intervals and immediately replaced by the same volume of fresh dissolution medium. The samples were assayed spectrophotometrically at λ max 286 nm and the concentration of the drug was determined from a previously constructed calibration curve. Experiments were carried out in triplicates; the results were averaged [16].

Drug release data analysis

To describe the kinetics of gatifloxacin release, data from the *in vitro* drug release study were fitted to different mathematical models such as zero-order, first order, Higuchi's model and Korsmeyer–Peppas model to evaluate the release mechanism of drug. The criterion for selecting the most appropriate model was based on a goodness-of-fittest [17].

Statistical analysis

The obtained data were analyzed statistically by the one-way analysis of variance (ANOVA) test at 95 % confidence level using Microsoft Excel 2010 software. The values were expressed in mean values±SD (Standard Deviation) of three replicates. Probability values of 0.05 or less ($p<0.05$) was considered statistically significant [18].

RESULTS AND DISCUSSION

Physical appearance of gel formulations

Prepared formulations were off-white to pale yellow(due to the color of the drug) viscous preparations, showing no phase separation, with smooth, aggregate free homogeneous texture with variable consistency ranging from liquid to thick gel preparations. Results are shown in table 2.

pH determination

The pH values of the prepared gels was found to be between 6.6 to 6.8 (table 2) which was well within the normal pH range of buccal cavity of 6 to 7;this is considered acceptable to avoid the risk of irritation upon application to oral mucosa.

Estimation of drug content

The data of drug content from all the prepared formulations show that the values range between 95.88 % and 100.58 %, representing

homogenous drug distribution throughout the gel. Results of drug content are shown in table 2.

Viscosity study

An important requirement for a gel for periodontal use is its viscosity. It should be in a range which will allow ease of application and permit the formulation to stay at site of application. There is no established criteria for the viscosity of periodontal gel, but a high viscose bio adhesive gel tend to retain at the site of application withstanding saliva washout and the mechanical stress while lower viscosity gels are easily administered to periodontal tissue by using a syringe.

Table 2: Physical properties of gatifloxacin periodontal gels

Formulation code	Appearance	pH	Drug content (%)
F 1	Clear, pale yellow liquid	Adjusted to 6.8	95.88±0.1
F 2	Clear, yellowish white viscous liquid	Adjusted to 6.8	98.70±0.2
F 3	Transparent, pale yellowish white gel	Adjusted to 6.8	99.88±0.33
F 4	Translucent yellow liquid	6.6±0.03	100.58±0.4
F 5	Translucent yellow gel	6.6±0.01	97.17±0.6
F 6	Translucent yellow gel	6.6±0.02	97.05±0.4
F 7	Yellow, transparent liquid	6.6±0.02	97.64±0.3
F 8	Yellow, transparent viscous liquid	6.6±0.01	96.88±0.6
F 9	Yellow, transparent viscous thick liquid	6.6±0.03	100.52±0.1
F 10	Translucent, pale yellow gel	Adjusted to 6.8	98.82±0.5
F 11	Translucent, pale yellow gel	Adjusted to 6.8	100.54±0.3
F 12	Translucent, pale yellow gel	Adjusted to 6.8	97.29±0.2
F 13	Translucent, pale yellow gel	Adjusted to 6.8	96.47±0.1
F 14	Translucent, yellow gel	6.67±0.02	99.41±0.3
F 15	Translucent, yellow gel	6.68±0.01	98.4±0.4

(Values represent mean±SD, n=3)

The obtained viscosity values of gatifloxacin gel formulations were in the range of 170–35850 mPa. s, as shown in table 3. For each of the three polymer studied (CP 940, CMC and HPMC), viscosity of the formulations was found to be affected by the type of polymer used although these polymers were not used at the same concentration ranges. Viscosity of gel formulations with carboxymethyl cellulose was high as compared to that of HPMC and carbopol. Furthermore, the viscosity of the formulations was found to be influenced by the concentration of polymers used; a significant increase ($p<0.05$) in viscosity was observed with increasing polymer concentrations. This may be due to higher degree of cross linking at higher concentrations of polymers. This is in accordance with results reported by Aslani *et al.* on their study on herbal gels as periodontal drug delivery system [19].

Formulations containing combinations of polymers (F10-F15), are more viscous then those containing only one polymer. Formulation F15 (3 % CMC and 10 % HPMC) exhibits highest viscosity (35850 mPa. s) whereas formulation F12 (1 % CP 940 and 5 % HPMC) exhibits lowest viscosity (2750 mPa. s). These results are in accordance with the finding of Biswas *et al.*[20] and Yellanki *et al.*[21].

Spreadability

The spreadability values for gatifloxacin periodontal gels ranged from (7.5-12.5) cm as shown in table 3, indicating ease of spreadability using small amount of shear.

Spreadability was not much influenced by the type of polymer used. However, data revealed that spreadability decreases with increasing polymer concentration as expressed by the lower diameter of the spread circle. Similar observations was shown by Helal *et al.* when formulating fluconazole topical gel using different polymers with different concentrations [22].

Formulations prepared using a combination of polymers (F10-F15) had lower spreadability values compared to formulations composed of only one polymer.

Table 3: Viscosity, spreadability and mucoadhesion test of gatifloxacin periodontal gel formulations

Formulation code	Viscosity (mPa. s) at 100 rpm	Spindle number	Spreadability diameter (cm)	Mucoadhesion test (distance moved, cm)
F 1	330±1.43	R5	12.5±0.3	>4
F 2	650±2.4	R5	11.5±0.4	1.5±0.2
F 3	3610±1.5	R5	11±0.2	0.1±0.1
F 4	1275±1.35	R5	12±0.1	0.9±0.3
F 5	6450±2.45	R7	11±0.5	0.5±0.2
F 6	25500±2.02	R7	8±0.3	0.3±0.1
F 7	170±1.14	R3	15±0.4	>4
F 8	2600±1.36	R7	12±0.2	>4
F 9	21150±1.79	R7	9.5±0.4	1.5±0.1
F 10	12100±1.66	R7	10±0.5	0.4±0.2
F 11	28050±2.55	R7	7.8±0.2	0.3±0.1
F 12	2750±1.08	R7	12±0.1	1±0.2
F 13	11000±2.4	R7	10.5±0.2	0.5±0.1
F 14	3850±1.8	R7	11±0.5	0.9±0.2
F 15	35850±2.6	R7	7.5±0.1	0.2±0.1

(Values represent mean±SD, n=3)

Bioadhesion study

Adhesive property is an important parameter in the design of periodontal gel, since a better clinical efficacy is obtained upon a good gel contact and retention at the mucosal surface. In the current study, the movement distance was used to determine the adhesive properties of the formulations on the agar plate. The shorter the movement distance, the better adhesion was between the polymer and the agar plate.

The effect of polymer type and concentration besides the effect of using a combination of polymers on the movement distance observed by different gel formulations on the agar plate are summarized in table 3.

Regarding the type and concentration of polymer, it was observed that the type of polymer will greatly affect bioadhesion and the movement distance of the formulation appeared to be inversely related to the polymer concentration; increasing the concentration of each polymer will provide better adhesion and hence longer residence time.

Ranking the bioadhesiveness in a descending order for each polymer was as follows: CMC (F6>F5>F4), CP 940 (F3>F2>F1) and HPMC (F9>F8>F7).

It is evident that movement distance of periodontal gels on the agar plate was influenced by their viscosities; higher viscosity gels tend to have longer residence time on agar and produce lower movement distance (table 3). This is in accordance with results reported by Songkro *et al.* on their study on nicotinamide oral gels [23].

Both CMC, a homo-polymer, and CP 940, a cross-linked polymer, form numerous hydrogen bonds due to their high molecular weights and their anionic nature (at buccal pH), which causes extensive swelling, changing their conformation and allowing for more agar-polymer interpenetration. However, the absence of cross-linking in CMC as compared to CP allows more freedom for diffusion and entanglement with agar making formulation based on CMC to have the best bioadhesion. HPMC based periodontal gels have the lowest bio-adhesive effect, due to the non-ionic nature and lower molecular weight of HPMC [24].

Formulations composed of a combination of polymers (F10-F15) showed a lower distance of movement on agar plate compared to their counterparts composed of single polymers; this means that there is a synergistic effect between polymeric combinations to increase bio adhesiveness: a favorable effect that causes retention of the formula to the site of application for the desired period of drug release. These results are in accordance with the finding of Roy *et al.* [25].

***In vitro* drug release study**

The release profile of gatifloxacin in McIlvaine buffer (pH 6.6) from different formulations was studied. For all formulations prepared, most of the gel dissolved within 6 h. The release profile was biphasic in nature, with an initial phase of high release (burst effect) followed by a second phase of moderate release. Burst release can be attributed to the drug which is present freely in the gel matrix. This was most evident for gels based on carbopol or HPMC. Considering the initial microbial load in the periodontal pocket, it is desirable to have a burst release of antimicrobial agents [26].

Graphical representation of release profile for periodontal gels prepared using a single polymer at different concentrations (F1-F9) is shown in fig.1. Drug release was significantly dependent on polymer type, and release profiles can be ranked in the following order: CP 940 (F1-F3)>HPMC (F7-F9)>CMC (F4-F6) where the amounts of the drug released after 120 min were 95-100% (F1-F3), 75-85 % (F7-F9) and 42-52 % (F4-F6), respectively. Formulation F1, which contained 0.75% CP 940, seemed to give the highest release rate of gatifloxacin among the formulations tested.

Regarding the polymer concentration, the graph demonstrates that increasing individual polymer concentration will decrease drug release rate. This may be due to the fact that increasing polymer concentration will increase viscosity of gels as well increasing polymer cross linking; this will reduce migration of drug molecules and decreased drug release. These results are similar to observations reported by Parhi *et al.* [27], Kalia *et al.* [28] and Mekkawy *et al.* [29].

In an attempt to enhance the drug release profile observed with gels based on CP or HPMC alone, gels were formulated using combination of polymers; namely gels composed of CMC/CP (F10-F11), HPMC/CP (F12-F13) and CMC/HPMC (F14-F15). Release profiles of these formulations were studied and are shown in fig. 2 with comparison to the release profile obtained when using single polymer formulas.

Gels containing 1 % carbopol alone (F2) produce significantly ($p<0.05$) higher drug release compared to gels containing combination of two polymers CMC/CP (F10, F11) and HPMC/CP (F12, F13). This could be due to the fact that carbopol undergo ionization at pH of the dissolution media and negative charges are developed along the backbone of the polymer leading to repulsion. Such an effect increases water uptake and causes the drug to diffuse from the formulation at a faster rate [30].

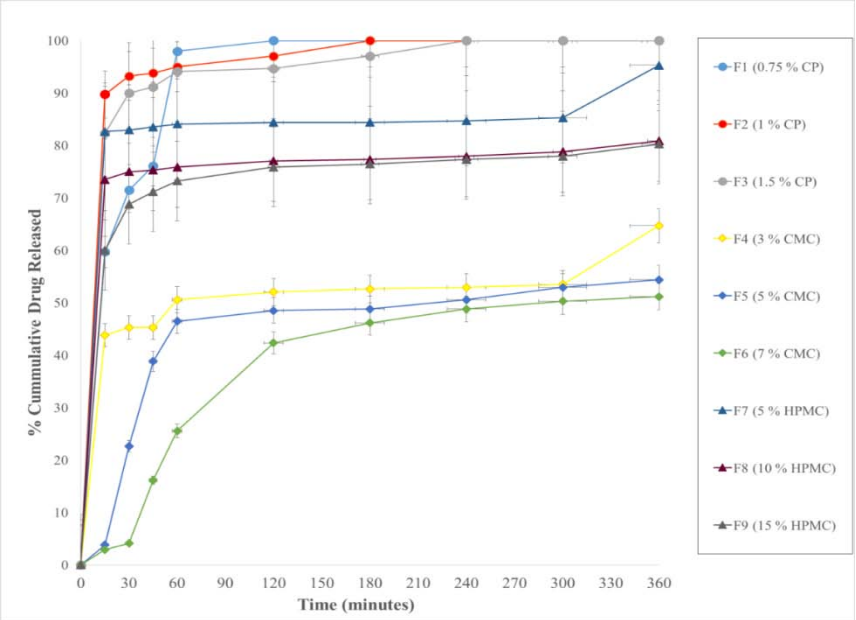

Fig. 1: Comparative drug release profiles of gatifloxacin periodontal gel formulations containing a single polymer (F1-F9)

For formulations produced by combining CMC with HPMC (F14 and F15), a significantly ($p<0.05$) higher drug release rate was observed when compared to formula containing 3 % CMC alone (F4) and a non-significant ($p>0.05$) higher drug release rate as compared to formulations containing HPMC alone (F7 and F8).

The increase in drug release rate was because of the hydrophilicity of this polymeric gel combination, and since F14 and F15 contain higher concentrations of HPMC than CMC, the release profiles obtained by them were closer to that seen with formulations containing 5 and 10 % HPMC (F7 and F8, respectively) than to formula F4 containing 3 % CMC alone.

It appears that periodontal gels of gatifloxacin prepared from binary polymeric mixtures exhibit different rates of drug release according to the nature of the gel-forming polymer as well as its concentration. As depicted in fig. 2, combination gels rich in HPMC (F12-F15) produced fast and poorly reproducible drug release profiles while combination gels based on CMC/CP (F10, F11) were able to produce a slower, more prolonged release profile of gatifloxacin extending for more than 6 h.

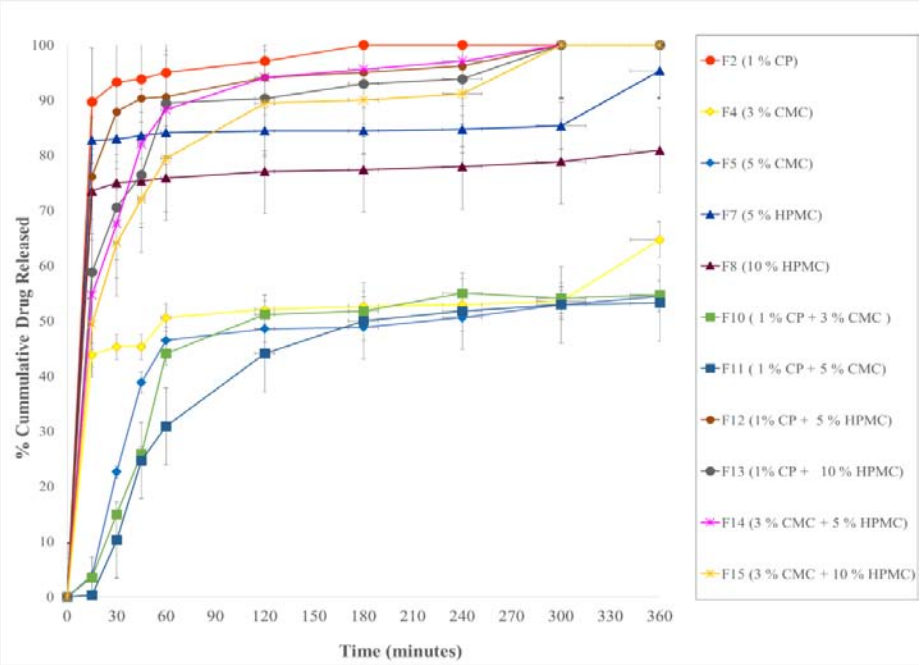

Fig. 2: Comparative drug release profiles of gatifloxacin periodontal gel formulations containing combination polymers (F10-F15) compared to corresponding formulations containing a single polymer

Drug release data analysis

In vitro drug release data were fitted to various release models, namely zero order, first order, Higuchi and Korsmeyer-Peppas. Results showed that drug release followed Higuchi model, this means that release of gatifloxacin from these formula was due to diffusion.

The release exponent value (*n*) for most of the formulations was less than 0.5, suggesting that the drug release followed Fickian diffusion mechanism, except for F5 and F10 which showed release exponent value between 0.5 and 1.0 indicating non-Fickian (anomalous) diffusion mechanism, the polymer relaxation rate being approximately equal to drug diffusion rate though polymer network; while F6 and F11 follow zero order drug release mechanism. However, zero order models are not suited to analyze swellable matrix systems, and were therefore rejected.

Among the Korsmeyer-Peppas equation and Higuchi models, by considering the higher correlation coefficient value (R^2), the release data seem to fit the Higuchi model better. The data is shown in table 4.

Table 4: Drug release model fitting of different gatifloxacin periodontal gel formulations to various kinetic models and their regression coefficients

Formulation code	Zero order	First order	Higuchi	Korsmeyer peppas		
	Correlation coefficient (R^2)	Correlation coefficient (R^2)	Correlation coefficient (R^2)	Correlation coefficient (R^2)	Release exponent (*n*)	Kinetic constant (k)
F1	0.7557	0.7394	0.8399	0.8973	0.2674	3.371
F2	0.9049	0.8943	0.9576	0.8943	0.0006	4.5095
F3	0.7474	0.7207	0.8401	0.9264	0.0554	4.2929
F4	0.8072	0.8175	0.7945	0.7909	0.0949	3.4965
F5	0.5277	0.3349	0.6616	0.6325	0.6125	0.7187
F6	0.7797	0.5871	0.8913	0.863	0.9318	1.1581
F7	0.5798	0.5913	0.4885	0.4006	0.0245	4.333
F8	0.9313	0.9287	0.9429	0.919	0.0248	4.2286
F9	0.6677	0.6283	0.7851	0.8817	0.0747	3.9524
F10	0.6182	0.439	0.7584	0.7578	0.7249	0.1251
F11	0.7344	0.3631	0.8626	0.667	1.2363	2.6033
F12	0.6995	0.6581	0.7995	0.8754	0.0701	4.2018
F13	0.7067	0.6517	0.8203	0.898	0.1527	3.7418
F14	0.6435	0.5828	0.7639	0.8586	0.1724	3.6572
F15	0.76	0.683	0.8739	0.9287	0.2018	3.4604

CONCLUSION

This study focused on the development of gatifloxacin containing gels for periodontal administration. The study has shown that by using different types of polymers or polymeric combinations and at different concentrations the rheological, bioadhesion and drug-release characteristics of prepared gels could be modified. The ideal formulation for the treatment of periodontitis shows good bio-adhesiveness, controlled drug release and ease of delivery into the periodontal pocket by topical application or by using a syringe. According to the obtained results, formulation F11 containing combination of 1 % CP and 5 % CMC could offer a compromise of adhesiveness, rheological and controlled release behaviors and is a good candidate for periodontal administration. Clinical studies of the gel preparation in healthy human volunteers should be evaluated in the future.

CONFLICTS OF INTERESTS

There are no conflicts of interest. The authors gratefully acknowledge Department of Pharmaceutics, College of Pharmacy in University of Baghdad for providing the equipment and most of the chemicals used in conducting this study.

REFERENCES

1. Jain N, Jain GK, Javed S, Iqbal Z, Talegaokar S, Ahmad FJ, *et al*. Recent approaches for the treatment of periodontitis. Drug Discovery Today 2008;13:932-43.
2. Vyas SP, Sihorkar V, Mishra V. Controlled and targeted drug delivery strategies towards intraperiodontal pocket disease. J Clin Pharm Ther 2000;25:21-42.
3. Jepsen K, Jepsen S. Antibiotics/antimicrobials: systemic and local administration in the therapy of mild to moderately advanced periodontitis. Periodontol 2016;71:82-112.
4. Iqbal Z, Jain N, Jain GK, Talegaonkar S, Ahuja A, Khar RK, *et al.* Dental therapeutic systems. Recent Pat Drug Delivery Formulation 2008;2:58-67.
5. Chhina K, Bhatnagar R. Local drug delivery. Indian J Dent Sci 2012;4:66-9.
6. Tariq M, Iqbal Z, Ali J, Baboota S, Talegaonkar S, Ahmad Z, *et al.* Treatment modalities and evaluation models for periodontitis. Int J Pharm Investig 2012;2:106–22.
7. Blondeau JM, Laskowski R, Bjamason, Stweart C. Comparative *in vitro* activity of gatifloxacin, grepafloxacin, levofloxacin, moxifloxacin and trovafloxacin against 4151 gram-negative and gram-positive organisms. Int J Antimicrob Agents 2000;14:45-50.
8. Varshosaz J, Tavakoli N, Saidian S. Development and physical characterization of a periodontal bioadhesive gel of metronidazole. Drug Delivery 2002;9:127–33.
9. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi Pharm J 2012;20:63–7.
10. Pawar DP, Shamkuwar PB. Formulation and evaluation of herbal gel containing *Lantana camara* leaves extract. Asian J Pharm Clin Res 2013;6:122-4.
11. Divya B, Sabitha P, Reddy R, Reddy M, Rao BN. An approach to enhance solubility of gatifloxacin by solid dispersion technique. Asian J Res Pharm Sci 2012;2:58-61.
12. Verma A, Singh S, Kaur R, Jain UK. Formulation and evaluation of clobetasol propionate gel. Asian J Pharm Clin Res 2013;6:15-8.
13. Garg A, Aggarwal D, Garg S, Singla AK. Spreading of semisolid formulations: an update. Pharmaceutical Technol 2002; 26:84–105.
14. Rao NR, Rao KP, Shivanand A, Reddy SR. Formulation, *in vitro* characterization and clinical evaluation of ofloxacinmedicated dental gels for periodontal infection. Int J Pharm Sci Nanotechnol 2012;5:1814-23.
15. Attia MA, El Badawy HY. Film forming gel for treatment of oral mucositis: *In vitro* studies. Int J Drug Delivery 2010;2:314-21.
16. Attia DA. *In vitro* and *in vivo* evaluation of transdermal absorption of naproxen sodium. Aust J Basic Appl Sci 2009;3:2154-65.
17. Costa P, Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci 2001;13:123–33.
18. Kumar L, Verma R. Chemical stability studies of bioadhesive topical gel. Int J Pharm Pharm Sci 2011;3:101-4.
19. Aslani A, Ghannadi A, Najafi H. Design, formulation and evaluation of a mucoadhesive gel from *Quercusbrantii L.* and *Coriandrumsativum L*. as periodontal drug delivery. Adv Biomed Res 2013;2:21.
20. Biswas GR, Majee SB, Roy A. Combination of synthetic and natural polymers in hydrogel: An impact on drug permeation. J Appl Pharm Sci 2016;6:158-64.
21. Yellanki SK, Nerella NK, Goranti S, Deb SK. Development of metronidazole intravaginal gel for the treatment of bacterial vaginosis: effect of mucoadhesive natural polymers on the release of metronidazole. Int J Pharm Tech Res 2010;2:1746-50.
22. Helal DA, El-Rhman DA, Abdel-Halim SA, El-Nabarawi MA. Formulation and evaluation of fluconazole topical gel. Int J Pharm Pharm Sci 2012;4:176-83.
23. Songkro S, Rajatasereekul N, Cheewasrirungrueng N. *In vitro* studies of mucoadhesiveness and release of nicotinamide oral gels prepared from bioadhesive polymers. World Acad Sci Eng Technol 2009;23:113-20.
24. Andrews GP, Laverty TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm 2009;71:505-18.
25. Roy A, Choudhury A, Bahadur S, Saha S. Phytoconstituent based mucoadhesive antifungal vaginal formulation: an effective and innovative approach. Biosci Biotechnol Res Commun 2016;9:694-701.
26. Nair RV, Nair SC. Cross linked chitosan in situ gel of sartanidazole for intra periodontal drug delivery. Int Res J Pharm 2014;5:384-91.
27. Parhi R, Terapalli BR, Teja B. Formulation and *in vitro* evaluation of minoxidil topical gel. Turk J Pharm Sci 2014; 11:153-62.
28. Kalia S, Singh P, Singh G, Gill NS. Development and characterization of erythromycin estolate emulgel for topical delivery. Int J Recent Adv Pharm Res 2014;4:31-50.
29. Mekkawy A, Fathy M, El-Shanawany S. Formulation and *in vitro* evaluation of fluconazole topical gels. Br J Pharm Res 2013;3:293-313.
30. Philip AK, Srivastava M, Pathak K. Buccoadhesive gels of glibenclamide: a means for achieving enhanced bioavailability. Drug Delivery 2009;16:405–15.
31. Ariyana A, Sinurat D, Ervina I, Bangun H. Formulation and *in vitro* evaluation of alginate based metronidazole periodontal gel. Asian J Pharm Clin Res 2014;7:223-7.

How to cite this article

- Hanan Jalal Kassab, Lena Murad Thomas, Saba Abdulhadi Jabir. Development and physical characterization of a periodontal bioadhesive gel of gatifloxacin. Int J Appl Pharm 2017;9(3):31-36.