Bangladesh Pharmaceutical Journal ***19****(2): 133-146, 2016*

Preparation and Evaluation of Ornidazole Periodontal Films

Jayera Islam Urmi, Marzia Alam and Md. Saiful Islam Pathan

Department of Pharmacy, State University of Bangladesh, Dhanmondi, Dhaka-1209, Bangladesh

Received: February 08, 2016; Accepted: March 29, 2016; Published (Web): July 31, 2016

Abstract

Periodontitis is a local infection in the gingival crevices, which affects the structural organs surrounding the teeth like periodontal ligament, connective tissue and bone. Ornidazole is an antimicrobial drug widely used to treat periodontitis. The primary objective of this study was to design and evaluate periodontal films of ornidazole for placement into the periodontal pockets for targeted delivery of drug. Nine formulations (F1 to F9) were prepared by solvent casting method using polymer A, polymer B and plasticizer A. Chloroform and dichloromethane were used as solvent system. The API and dental films were then evaluated for various parameters including trinocular microscopic image, melting point, weight variation, thickness, folding endurance, surface pH, swelling index, percentage moisture loss, antimicrobial activity, content uniformity, *in vitro* drug release and release kinetics as well as RTIR and DSC. Formulation F1 showed the minimum weight and thickness and F9 showed the maximum. It was observed that weight and thickness of film were directly proportional to the total solid content of the film. RSDs of content uniformity test for all the batches were below 3.0%. Folding endurance and swelling index of films were inversely proportional to the amount of polymer in the film. The surface pH of all the batches were between 6-7. Formulation F1 revealed the maximum percentage of moisture loss (19.34%), while F8 showed the minimum (3.654%). Formulation F2 demonstrated data the highest zone of inhibition (21.91 mm).

Key words: Preparation, Evaluation, Ornidazole, Periodontal film, Periodontitis, Solvent casting.

Introduction

Dental diseases are recognized as one of the major public concerns throughout the world. The most common form of periodontal disease include gingivitis and periodontitis (Figure 1). Periodontal literally means "around the tooth". Periodontitis = Peri + odont + itis where “Peri” = around, “odont” = tooth and “itis” = inflammation. Hence, it refers to a number of inflammatory diseases affecting the periodontium, the supporting tissues around the teeth (Nair *et al*., 2012). It can affect one tooth or several teeth and if left untreated and may lead to tooth loss. In the early stages, only the gums are infected (gingivitis). Later, it spreads to the bone surrounding the tooth and other supporting tissues. Finally, the tooth becomes loose and may fall out. The clinical signs include changes in the morphology of gingival tissues, gingival bleeding as well as periodontal pocket formation (Armitage *et al*., 2004). This pocket (Figure 2) provides an ideal environment for the growth and proliferation of anaerobic pathogenic bacteria. Periodontal disease can affect people of any age.

Periodontitis is a multifactorial infection with great complexity in the mechanism of pathogenesis and caused by microorganisms that adhere on the tooth's surfaces. Periodontal disease is associated with a variable microbial pattern. Anaerobic species of bacteria including *Porphyromonas gingivalis, Bacteroides forsythus, Treponema denticola, Prevotella intermedia, Fusobacterium nucleatum, Eubacterium* sp.— have been implicated in chronic periodontitis. Microaerophile bacteria including *Actinomyces actinomycetemcomitans, Campylobacter rectus,* and *Eikenella corrodens* may also play a role in chronic periodontitis. So the treatment of periodontitis mainly

Correspondence to: Md. Saiful Islam Pathan; Email: sip@sub.edu.bd

focuses on the reduction of the total bacterial count by the use of antimicrobials.

Peridental films have may advantages over conventional dosge from including, targeted drug delivery, less storage space, less maintenance of machineries and less HVAC investment (Sharma Nishu *et al.*, 2013; Nair *et al*., 2012).

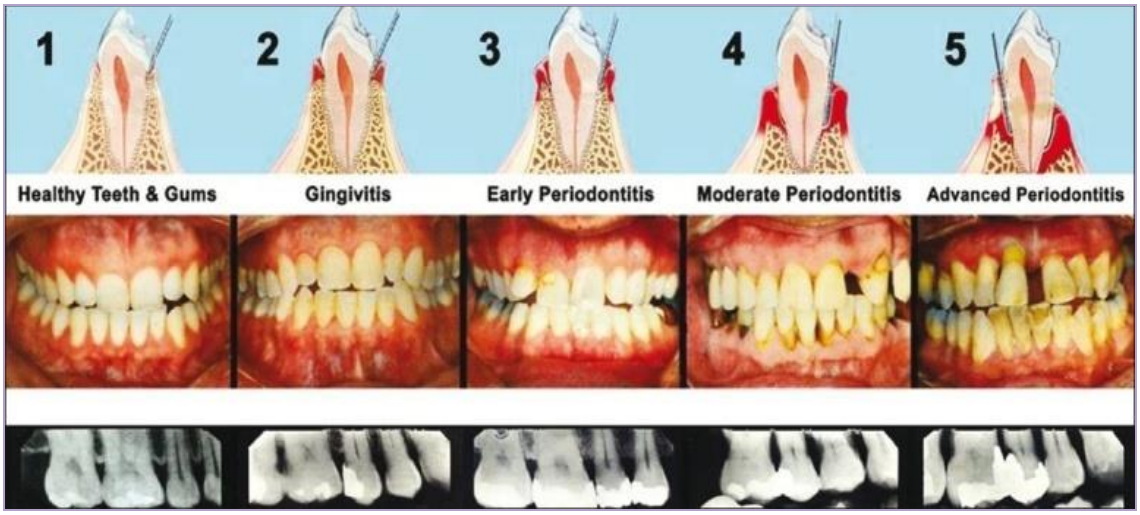

Figure 1. Different stages of periodontitis.

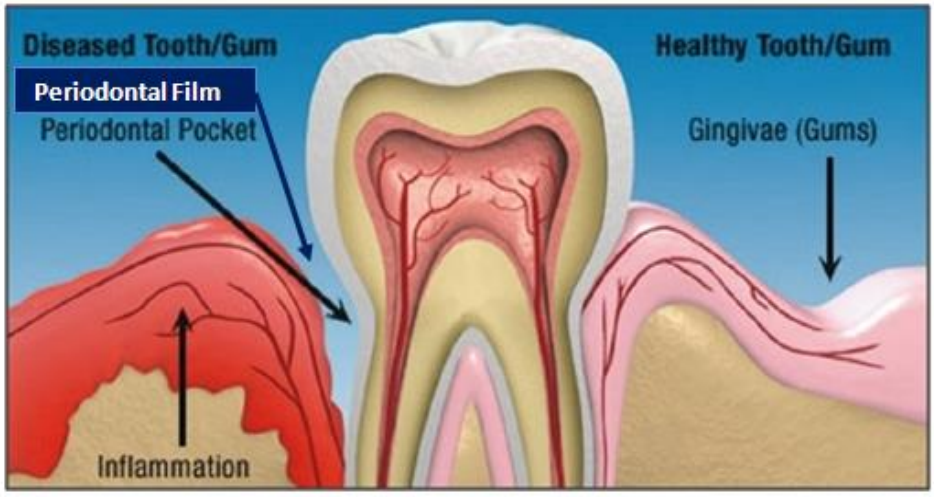

Figure 2. Periodontal pocket.

Materials and Methods

Ornidazole was obtained as a gift sample from Opsonin Pharmaceuticals Ltd., Bangladesh. Polymer A was obtained from Colorcon, Germany and Polymer B was obtained from Evonik Industries, Germany. Chloroform and dichloromethane were purchased from Merck, India. Other ingredients used were of analytical grade.

Fabrication of ornidazole dental films by solvent casting method

The films were prepared by solvent casting technique (Vineetha *et al*., 2015; Tasneem *et al.*, 2015; Kumar *et al*., 2013; Shankraiah *et al*., 2011; Prabhushankar *et al*., 2010). Nine batches (F1 to F9) with various compositions of films were casted (Table 1). The required quantity of polymer A was added

slowly in 1:1 mixture of chloroform & dichloromethane with continuous stirring using glass rod. When polymer A was dissolved completely in the solvent, required quantity of polymer B was added slowly to the mixture to form uniform clear viscous solution. An accurately weighed ornidazole was then incorporated in the polymeric solution after adding plasticizer A. The mixture was then stirred until a homogenous mixture of drug and polymer was achieved. Then this polymeric solution containing drug was casted on a petridish and allowed to dry at room temperature for 1 hour 40 minutes. After evaporation of solvent, the dried film was peeled out from the petridish and cut into desired size (10×2 mm^2) and shape and stored in air tight packets.

Table 1. Composition of Ornidazole dental film formulations using different levels of polymer A and polymer B.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ornidazole (mg)	0.685	0.685	0.685	0.685	0.685	0.685	0.685	0.685	0.685
Polymer A (mg)	4.5	5.25	6.0	6.75	7.5	8.25	9.0	9.75	10.5
Polymer B (mg)	2.0	2.0	2.0	2.5	2.5	2.5	3.0	3.0	3.0
Drug : Polymer	1: 9.5	1: 10.6	1: 11.7	1: 13.5	1: 14.6	1: 15.7	1: 17.5	1: 18.6	1: 19.7
Plasticizer A (mg)	1.410	1.410	1.410	1.410	1.410	1.410	1.410	1.410	1.410
Chloroform (ml)	0.053	0.053	0.053	0.053	0.053	0.053	0.053	0.053	0.053
Dichloromethane (ml)	0.053	0.053	0.053	0.053	0.053	0.053	0.053	0.053	0.053

Preformulation studies

The following prefomulation studies were performed for drug and polymers:

Melting point determination of ornidazole: Melting point of pure ornidazole was determined by capillary tube method and the temperature range at which the drug melted was recorded.

Fourier Transform Infrared (FTIR) Spectroscopy of pure drug: The pure drug ornidazole was subjected to FTIR studies alone. Sample of pure drug (approximately 2-3 mg) was placed in the sample holder of the instrument and analyzed between 4000 and 400cm^{-1} to obtain the FTIR spectrum.

Differential Scanning Calorimetry (DSC) of pure drug: DSC was employed to study any potential change in ornidazole that the drug may have experienced during its processing into periodontal films. DSC thermogram was obtained using thermal analyzer instruments (DSC- 60, Shimadzu, Japan). Prior to analysis, the instrument was calibrated using an indium standard. The sample was crumped in aluminium cells and heated at a rate of 10°C minute in an atmosphere of nitrogen (Hasan *et al.*, 2014).

Evaluation of the films

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

Morphological properties of dental films: All films were visually inspected for properties such as colour, clarity, flexibility, transparency and smoothness (Alam *et al*., 2014).

Weight uniformity of dental films: Film (size of 10×2 mm^2) was taken from different areas of film and the weight variation of each film was determined (Tasneem *et al.*, 2015; Alam *et al.*, 2014).

Thickness uniformity of dental films: The thickness of each film was measured using screw gauge (thickness tester) at different positions of the film and the average was calculated (Tasneem *et al.*, 2015; Alam *et al.*, 2014; Kumar *et al*., 2013).

Folding endurance of dental films: The folding endurance of the films was determined by repeatedly folding a small strip of film of 20×10 mm^2 at the same place till it broke or folded up to 300 times, which is considered satisfactory to reveal good film properties

(Tasneem *et al.*, 2015; Alam *et al.*, 2014; Shankraiah *et al*., 2011).

Surface pH of dental films: Periodontal films were left to swell for 1 hour on the surface of the agar plate, prepared by dissolving 2% w/v agar in warm phosphate buffer solution, at pH 6.8 under stirring and then poured into the petridish till gelling/solidification 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 were recorded (Tasneem *et al.*, 2015; Kumar *et al*., 2013; Aviral *et al*., 2012).

Swelling index (SI) of dental films: Periodontal films were individually weighed (W_1) and placed in an agar plate, stirred and the solution was poured into the petridish till it solidified at room temperature and examined for increase in weight. After 15 minutes intervals for 1 hour, films were removed from the gel plates and excess surface water was removed carefully using tissue paper. The swollen films were then reweighed (W_2), and the swelling index (SI) was calculated using the following formula (Sharma *et al*., 2013). The swelling index was calculated by using the following formula-

$$SI = ((W_2 - W_1) / W_1) \times 100$$

Where,

W_1 = the weight of film at time zero

W_2 = the weight of swollen film

Percentage moisture loss (PML) of dental films: Percentage moisture loss was determined by keeping the films (10×2 mm^2) in a desiccator containing anhydrous calcium chloride (Kumar *et al*., 2013; Aviral *et al*., 2012). After 3 days, the films were taken out, re-weighed and the percentage moisture loss was calculated using the following formula-

Percentage moisture loss (PML) = ((Initial weight – Final weight) / Initial weight) × 100

Assay/drug content and uniformity of drug content in dental films: A film (10×2 mm^2) of known weight was taken in 10 ml volumetric flask and 10 ml of acetone was added and sonicated for 15 minutes. The solution was then filtered with Whatman filter paper number 1.0 ml of the filtrate was taken in another 10 ml volumetric flask and diluted with phosphate buffer of pH 6.8 and absorbance was recorded at 318 nm. The polymeric solution without drug served as blank (Alam *et al.*, 2014; Shankraiah *et al*., 2011).

Antibacterial activity of dental films: Antibacterial activity of ornidazole dental film was evaluated by comparing with standard metronidazole disc. It was performed on all formulations by placing the films (10×2 mm^2) on agar plates seeded with *E. coli* . After 24 hours of incubation at 37°C, the films were observed to determine the zone of inhibition (Shankraiah *et al*., 2011).

In vitro drug release of dental films: In vitro drug release was performed by placing the films of known weight and dimension (10×2 mm^2) into small test tubes containing 2 ml of phosphate buffer solution, at pH 6.8. The test tubes were sealed with aluminium foil and kept at 37 ^oC for 24 hours. 1 ml of buffer was withdrawn and immediately replaced with a fresh 1 ml phosphate buffer solution (pH 6.8) after 24 hours. The withdrawn samples were suitably diluted and the concentration of drugs in the buffer was measured at 318 nm. The studies were performed (24 hours, 48 hours, 72 hours upto 96 hours) and triplicate data of each absorbance was noted (Kumar *et al*., 2013; Aviral *et al*., 2012).

Release kinetics of dental films: The *in vitro* release data obtained from various formulations of ornidazole dental films were fitted to various kinetic models such as zero order, first order, Higuchi model, Korsmeyer-Peppas model and Hixson-Crowell model (Hasan *et al.*, 2014; Aqther *et al*., 2013; Kumar *et al*., 2013; Shankraiah *et al*., 2011; Mastiholimath *et al*., 2006).

Fourier Transform Infrared (FTIR) spectroscopy of dental films: The dental films were subjected to FTIR studies. Samples of drug-polymer combination (film) for FTIR was placed in the sample holder of the instrument and analyzed between 4000 and 400cm^{-1} to assess for incompatibilities of drug with polymer.

Trinocular microscopic imaging of dental films: Trinocular microscopic imaging of ornidazole dental film was carried out. The surface of the film and distribution of polymer and drug within the film was examined (Tasneem *et al.*, 2015; Alam *et al.*, 2014).

Results and Discussion

Melting point determination of ornidazole: Melting point of pure ornidazole was determined by capillary tube method. The temperature at which the drug melted was found to be 85 °C to 87 °C.

Morphological properties of dental films: Polymers used for the fabrication of periodontal films showed good film forming property and reproducibility. The results of visual inspection of films showed that all the film formulations from F1 to F9 were transparent having smooth upper surface and rough lower surface.

Weight uniformity of dental films: Drug loaded films (10×2 mm^2) were tested for uniformity of weight. The results of weight uniformity showed that the films were found uniform in weight. The average weight of the films was found in the range of 6.15 mg to 10.68 mg. Maximum average weight was found for formulation F9 (10.68 mg) and minimum for formulation F1 (6.15 mg). Figure 3 is a comparative chart showing mean weight of different film formulations (from F1 to F9). From the graph, it is quite evident that weight of the film is directly proportional to the amount of polymer in each formulation.

Thickness uniformity of dental films: All the films were evaluated for thickness uniformity. The average thickness of films were found in the range of 242.8 µm to 399.9 µm. Maximum average thickness was found for formulation F9 (399.9 µm) and minimum for formulation F1 (242.8 µm). Figure 4 is a comparative chart showing mean thickness of different film formulations (from F1 to F9). From the graph, it is clear that thickness of the film is directly proportional to the amount of polymer in each formulation.

Folding endurance of dental films: The folding endurance was measured manually by folding the films (20×10 mm^2) repeatedly at a point till they broke. The average folding endurance was found in the range of 117 to 334 times. Maximum folding endurance was found for formulation F1 (334 times) and minimum for formulation F9 (117 times). Figure 5 is a comparative chart showing folding endurance of different film formulations (from F1 to F9). From the graph, it is quite evident that folding endurance of the film is inversely proportional to the amount of polymer in each formulation.

Surface pH of dental films: All the prepared formulations (F1 to F9) of ornidazole dental films showed the pH range within 6.5 to 6.8. The observed surface pH of formulations F1, F2, F3, F4, F5, F6, F7, F8 and F9 were 6.5, 6.8, 6.6, 6.8, 6.5, 6.8, 6.6, 6.8 and 6.7 respectively. The result shows that there is no significant difference of surface pH in all the formulations.

Swelling index (SI) of dental films: All the prepared formulations (F1 to F9) of ornidazole dental films were evaluated for swelling index. The swelling index was found maximum for formulation F1 (49.19%) and minimum for formulation F9 (7.83%). Figure 6 is a comparative chart showing swelling index of different film formulations (from F1 to F9). From the graph, it is quite evident that the swelling index decreased with increased amount of polymer.

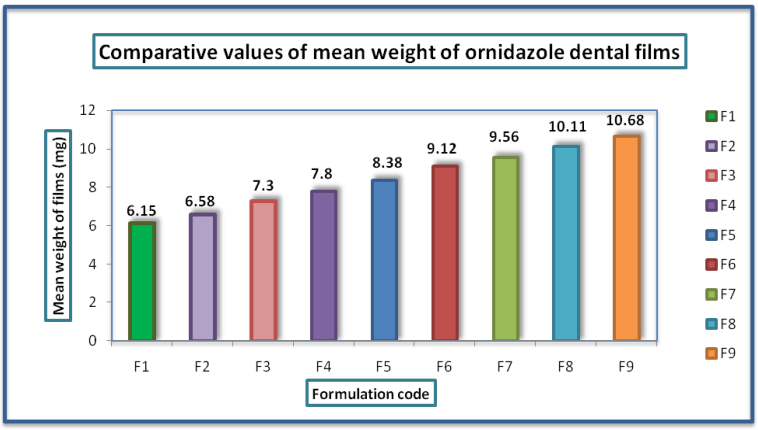

Figure 3. Comparative mean weight of formulations F1 to F9.

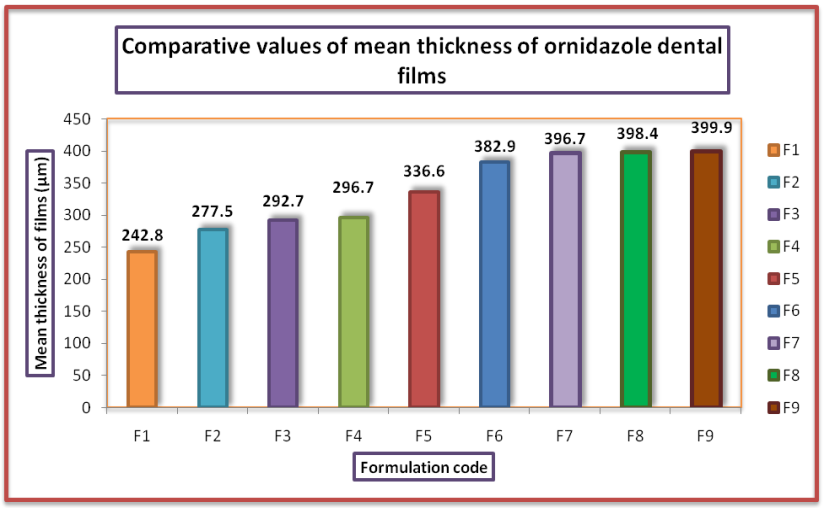

Figure 4. Comparative mean thickness of formulations F1 to F9.

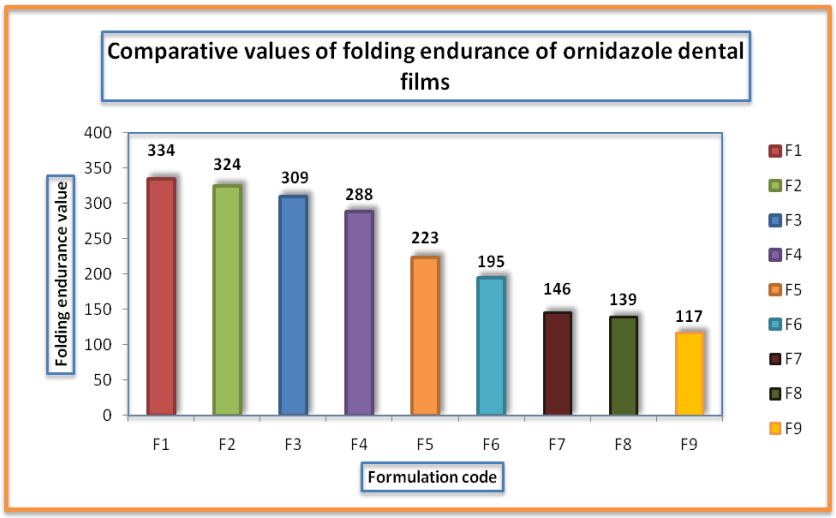

Figure 5. Comparative folding endurance of formulations F1 to F9.

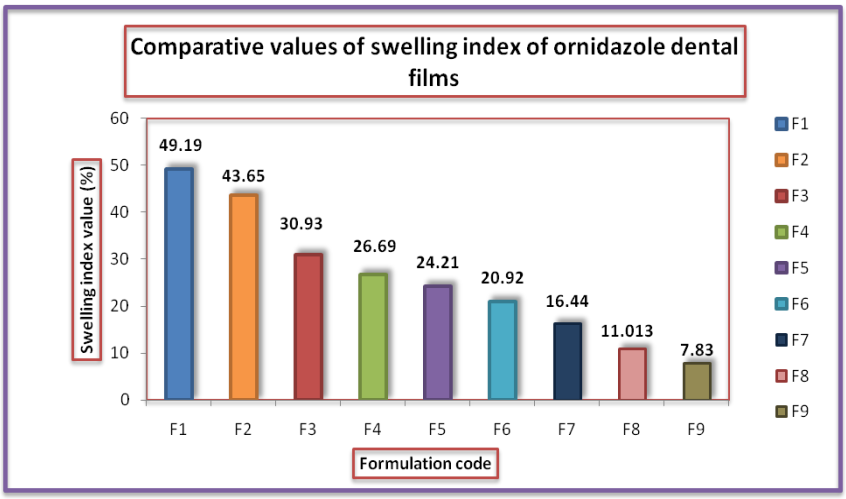

Figure 6. Comparative swelling index of formulations F1 to F9.

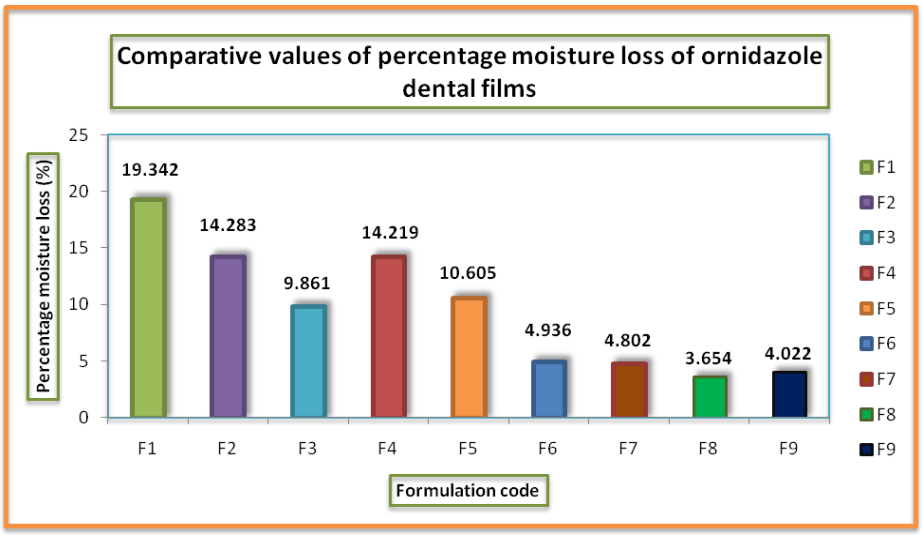

Figure 7. Comparative mean percentage moisture loss of formulations F1 to F9.

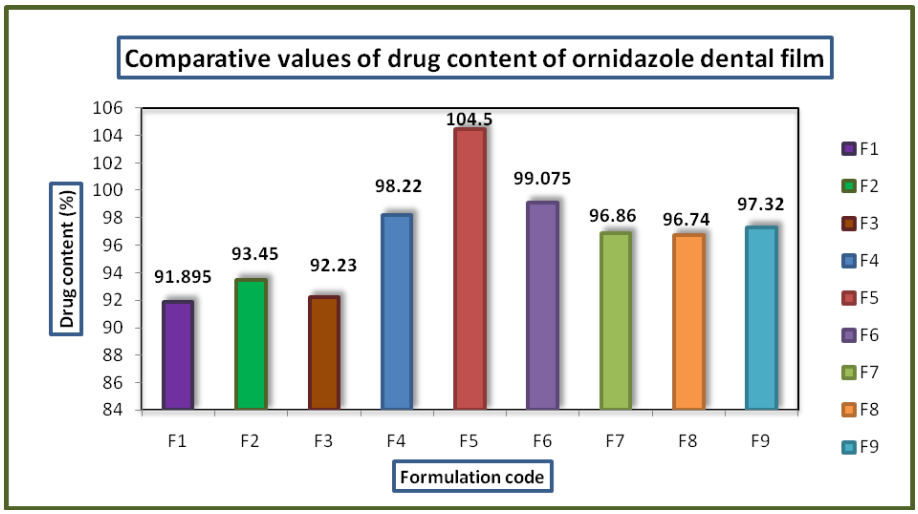

Figure 8. Comparative mean drug content of formulations F1 to F9.

Percentage moisture loss (PML) of dental films: All the prepared formulations (F1 to F9) of ornidazole dental films were evaluated for percentage moisture loss. The average percentage moisture loss of the films was found in the range of 3.654% to 19.342%. Maximum average percentage moisture loss was found for formulation F1 (19.342%) and minimum for formulation F8 (3.654%). Figure 7 is a comparative chart showing mean percentage moisture loss of different film formulations (from F1 to F9).

Assay/ drug content & drug content uniformity of dental films: All the prepared formulations (F1 to F9) of ornidazole dental films were evaluated for assay & drug content uniformity. From the results of assay & drug content uniformity, it is quite evident that all the batches (F1 to F9) have RSD values less than 3% which indicates uniform distribution of the API i.e ornidazole throughout the dental film and thus complies with the content uniformity test.

Figure 8 is a comparative chart showing drug content of different film formulations (from F1 to F9).

Antibacterial activity of dental films: All the prepared formulations (F1 to F9) of ornidazole dental films were evaluated for antibacterial activity determining the zone of inhibition for each film. The

results of zone through inhibition are given in table 2. The antibacterial activity of the films was found in the range of 14.89 mm to 24.25 mm in major axis and 9.37 mm to 19.53 mm in minor axis. Maximum antibacterial activity was found for formulation F2 (24.25 mm in major axis and 19.53 mm in minor axis) and minimum for formulation F9 (14.89 mm in major axis and 9.37 mm in minor axis). So, it is quite evident from table 2 that formulation with the maximum amount of polymer has the minimum zone of inhibition.

In vitro drug release of dental films: The results of *in vitro* release studies of different formulations are shown in figure 10 where the cumulative percentage release vs time (hours) graph was plotted. Figure 9 shows the comparative cumulative drug release from different film formulations (F1 to F9) of ornidazole dental films. Formulation F1 showed 100% drug release over a period of 48 hours which may be due to the minimum amount of polymer in the formulation whereas formulation F9 showed 87.15% drug release over a period of 96 hours which may be due to maximum amount of polymer in the formulation. So, it is quite evident from the *in vitro* release study that the more the polymer in the formulation, the less the drug release from the formulated film.

Table 2. Antibacterial activity of F1 to F9 formulations of ornidazole dental films.

Formulation code	Zone of inhibition (mm)	
	Major axis (mm)	Minor axis (mm)
F1	21.91	18.21
F2	24.25	19.53
F3	21.65	18.38
F4	19.65	15.85
F5	17.62	13.51
F6	20.18	18.53
F7	18.14	15.45
F8	15.38	10.41
F9	14.89	9.37

Release kinetics of dental films: Data obtained from *in vitro* release studies of various formulations (F1 to F9) of ornidazole dental films were fitted to various kinetic equations such as zero order, first order, Higuchi model, Korsmeyer-Peppas model and Hixson-Crowell model. The results are presented in table 3 to 7.

Formulation F1, F2 and F3 containing drug polymer ratio of 1:9.5, 1:10.6, 1:11.7 showed drug release of 100.534%, 100.556% and 107.47%, respectively, after 72 hours. Formulation F4, F5, F6, F7, F8 and F9 containing drug polymer ratio of 1:13.5, 1:14.6, 1:15.7, 1:17.5, 1:18.6 and 1:19.7 deplayed drug release of 109.07% , 101.48% , 96.26% , 94.66% , 90.92% and 87.15%, respectively after 96 hours.

Initially all the formulations were compared with the zero order or first order release kinetics to define whether the process is concentration dependent or concentration independent process (Kumar *et al*., 2013). The R^2 (regression/ correlation coefficient) values as shown in table 8 indicates that formulation F1 to F3 had higher R^2 values for the first order release than the zero order. Thus, it can be concluded that the drug release of formulation F1 to F3 is concentration dependent process. On the other hand, formulation F4 to F9 had higher R^2 values for the zero order release than first order which means that the drug release of formulation F4 to F9 follows concentration independent process.

Further studies were performed to determine the nature of the release pattern of drug from the films and the drug release data were fitted to various release kinetic models like Higuchi's model, Korsmeyer-Peppas model and Hixon-Crowell's cubic root law models (Kumar *et al*., 2013; Shankraiah *et al*., 2011). The data that are obtained from the study enlisted in table 9 indicates that R^2 values are higher for Korsmeyer-Peppas model compared to Higuchi's model and Hixon-Crowell's model for all the formulations except F2. The Korsmeyer-Peppas model was found to be linear with the R^2 values of 1, 0.996, 1, 0.999, 0.999, 0.998, 0.987, 0.999 and 0.999 for formulation F1, F2, F3, F4, F5, F6, F7, F8 and F9 respectively (Mastiholimath *et al*., 2006). The diffusional exponent (n) values for Korsmeyer-Peppas model (Table 10) were found to be within 0.319 to 0.416, hence the release pattern mainly indicated as the fickian diffusion type (Costa *et al*., 2001).

Table 3. Zero order release profile of formulations F1 to F9 of ornidazole dental films.

Time (hours)	Cumulative % release of drug								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
24	61.498	48.67	45.98	39.56	36.79	32.61	33.17	29.40	29.40
48	100.534	78.626	77.51	65.22	62.45	55.62	50.28	52.41	50.25
72		100.556	107.47	90.88	85.98	75.94	75.94	74.34	70.57
96				109.07	101.48	96.26	94.66	90.92	87.15

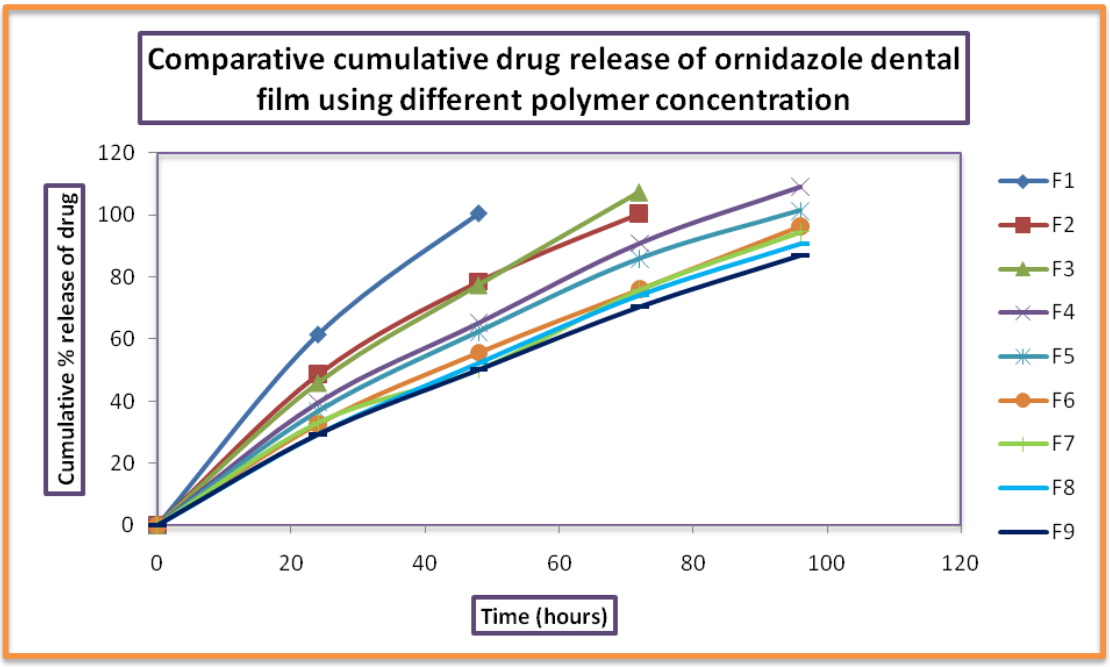

Figure 9. Comparative cumulative % drug release of ornidazole dental film using different polymeric concentration.

Table 4. First order release profile of formulations F1 to F9 of ornidazole dental films.

Time (hours)	Log drug % remaining								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	2	2	2	2	2	2	2	2	2
24	1.585	1.710	1.733	1.781	1.801	1.829	1.825	1.849	1.849
48		1.3299	1.352	1.541	1.575	1.647	1.697	1.678	1.697
72				0.96	1.147	1.381	1.381	1.409	1.469
96						0.573	0.728	0.958	1.109

Table 5. Higuchi release profile of formulations F1 to F9 of ornidazole dental films.

SQRT (hours)	Cumulative % release of drug								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
4.899	61.498	48.67	45.98	39.56	36.79	32.61	33.17	29.40	29.40
6.928	100.534	78.626	77.51	65.22	62.45	55.62	50.28	52.41	50.25
8.485		100.556	107.47	90.88	85.98	75.94	75.94	74.34	70.57
9.798				109.07	101.48	96.26	94.66	90.92	87.15

Table 6. Korsmeyer-Peppas profile of formulations F1 to F9 of ornidazole dental films.

Log time (hours)	Log cumulative % release of drug								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.380	1.789	1.687	1.663	1.597	1.566	1.513	1.521	1.468	1.468
1.681	2.002	1.896	1.889	1.814	1.796	1.745	1.701	1.719	1.701
1.857		2.002	2.031	1.958	1.934	1.880	1.880	1.871	1.849
1.982				2.038	2.006	1.983	1.976	1.959	1.940

Table 7. Hixson-Crowell profile of formulations F1 to F9 of ornidazole dental films.

Time (hours)	Cubic root of drug remaining (%)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	4.642	4.642	4.642	4.642	4.642	4.642	4.642	4.642	4.642
24	3.377	3.716	3.780	3.924	3.983	4.069	4.058	4.133	4.133
48		2.775	2.823	3.264	3.349	3.540	3.677	3.624	3.678
72				2.089	2.411	2.887	2.887	2.9495	3.087
96						1.552	1.748	2.086	2.342

Table 8. R^2 values for zero order and first order release kinetics of formulations F1 to F9 of ornidazole dental films.

Formulation Code	Zero order release kinetics	First order release kinetics	Best Fitted
	R^2	R^2	
F1	0.983	1	First order
F2	0.967	0.994	First order
F3	0.988	0.989	First order
F4	0.980	0.937	Zero order
F5	0.977	0.963	Zero order
F6	0.988	0.870	Zero order
F7	0.988	0.891	Zero order
F8	0.989	0.944	Zero order
F9	0.988	0.960	Zero order

Table 9. R^2 values for Higuchi, Korsmeyer-Peppas and Hixson-Crowell release kinetics of formulations F1 to F9 of ornidazole dental films.

Formulation code	Higuchi release kinetics	Korsmeyer-Peppas release kinetics	Hixson-Crowell release kinetics	Best fitted
	R^2	R^2	R^2	
F1	0.988	1	1	Korsmeyer-Peppas, Hixson-Crowell
F2	0.989	0.996	1	Hixson-Crowell
F3	0.971	1	0.999	Korsmeyer-Peppas
F4	0.973	0.999	0.980	Korsmeyer-Peppas
F5	0.975	0.999	0.990	Korsmeyer-Peppas
F6	0.964	0.998	0.956	Korsmeyer-Peppas
F7	0.956	0.987	0.96	Korsmeyer-Peppas
F8	0.959	0.999	0.985	Korsmeyer-Peppas
F9	0.964	0.999	0.990	Korsmeyer-Peppas

Table 10. Correlation coefficient (R^2) values & diffusional exponent (n) values for Korsmeyer-Peppas release kinetics of formulations F1 to F9 of ornidazole dental films.

Formulation code	Korsmeyer-Peppas release kinetics	
	Correlation coefficient value (R^2)	Diffusional exponent value (n)
F1	1	0.416
F2	0.996	0.375
F3	1	0.375
F4	0.999	0.354
F5	0.999	0.346
F6	0.998	0.332
F7	0.987	0.329
F8	0.999	0.324
F9	0.999	0.319

Fourier Transform Infrared (FTIR) Spectroscopy: The pure drug ornidazole and dental films were subjected to FTIR studies. The FTIR spectrum of pure ornidazole and ornidazole with polymers (film) is shown in figures 10 and 11.

FTIR spectra of pure drug (Figure 10) shows prominent peaks at 3165.19 cm $^{-1}$, 3116.97 cm^{-1} and 3091.89 cm^{-1}, 1533.41 cm^{-1}, 1357.89 cm^{-1}, 1149.57 cm^{-1}, 879.54 cm^{-1} corresponding to –OH stretching, -CH stretching, asymmetric -NO_2 streching, symmetric -NO_2 streching, -CO stretching, -CN, -NO_2 streching, respectively. The FTIR spectra of drug in combination with polymer **(**Figure 11), was found at 3178.69 cm^{-1}, 3103.46 cm^{-1} and 3037.89 cm^{-1}, 1531.48 cm^{-1}, 1371.39 cm^{-1}, 1060.85 cm^{-1}, 879.54 cm^{-1}.

FTIR studies of film shows slight changes in peaks, which needs further study.

Differential Scanning Calorimetry (DSC) of pure drug: DSC was employed to study any potential change in ornidazole that the drug may have experienced during its processing into periodontal films. Thermal analysis of the pure drug was done to see the melting point of drug. It was found 87.12°C. The thermogram of ornidazole is shown in figure 12.

Trinocular microscopic imaging of dental films: Images of ornidazole dental films were taken by

trinocular microscope. The surface of the film and distribution of polymers and drug within the film was examined. From figure 13, it appears that the drug molecule is uniformly distributed in polymers which supports the content uniformity test.

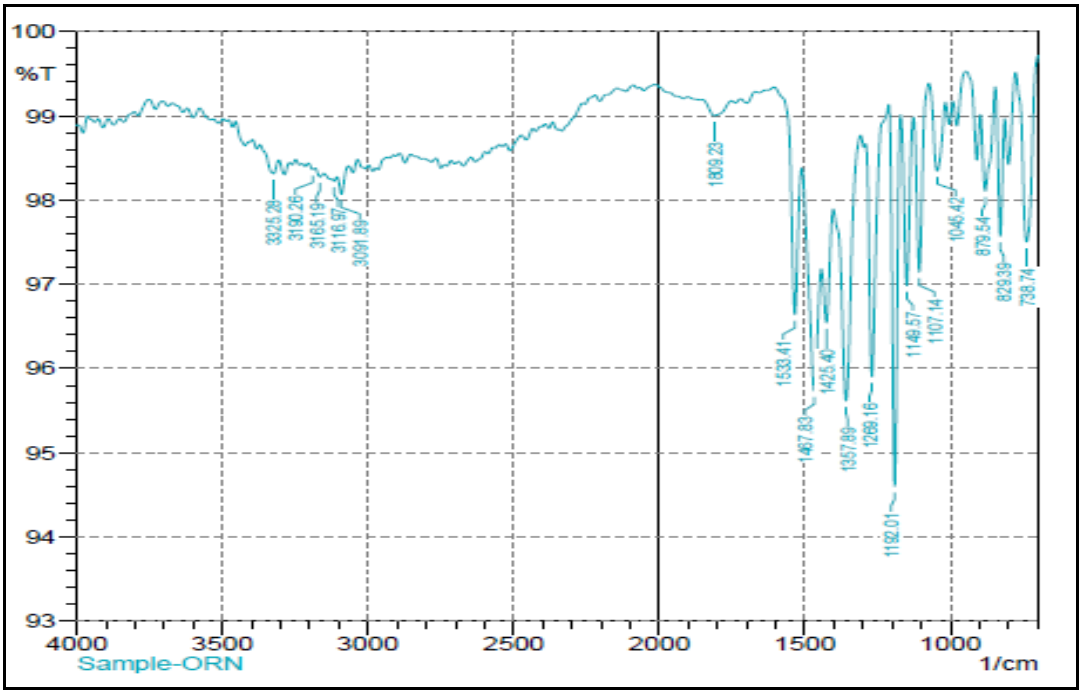

Figure 10. FTIR spectrum of pure ornidazole.

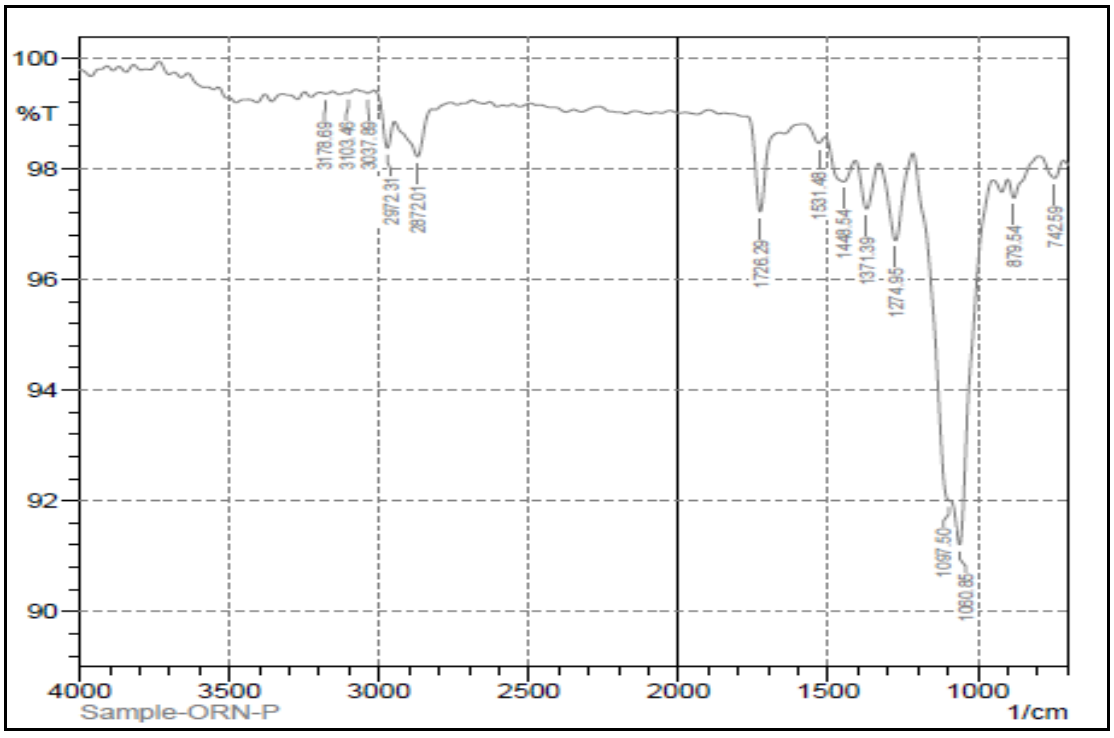

Figure 11. FTIR spectrum of ornidazole dental film.

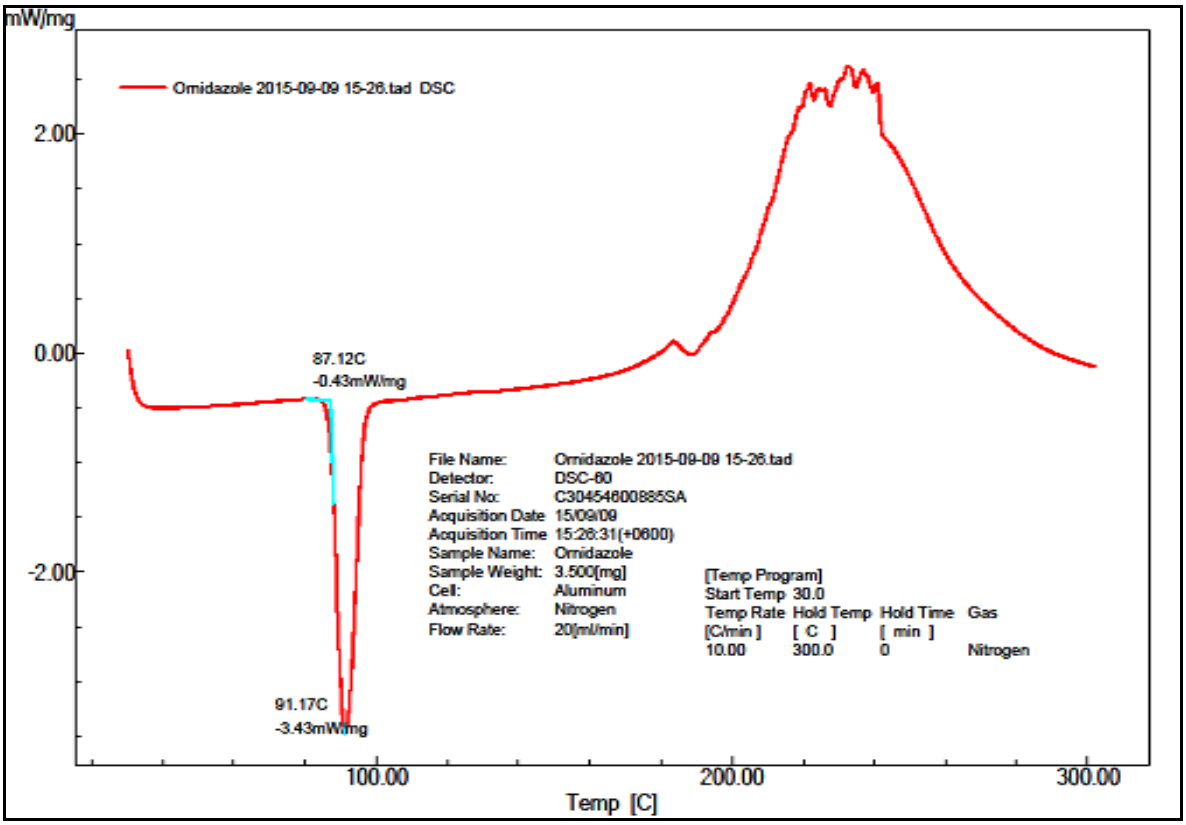

Figure 12. DSC curve showing melting point of pure ornidazole.

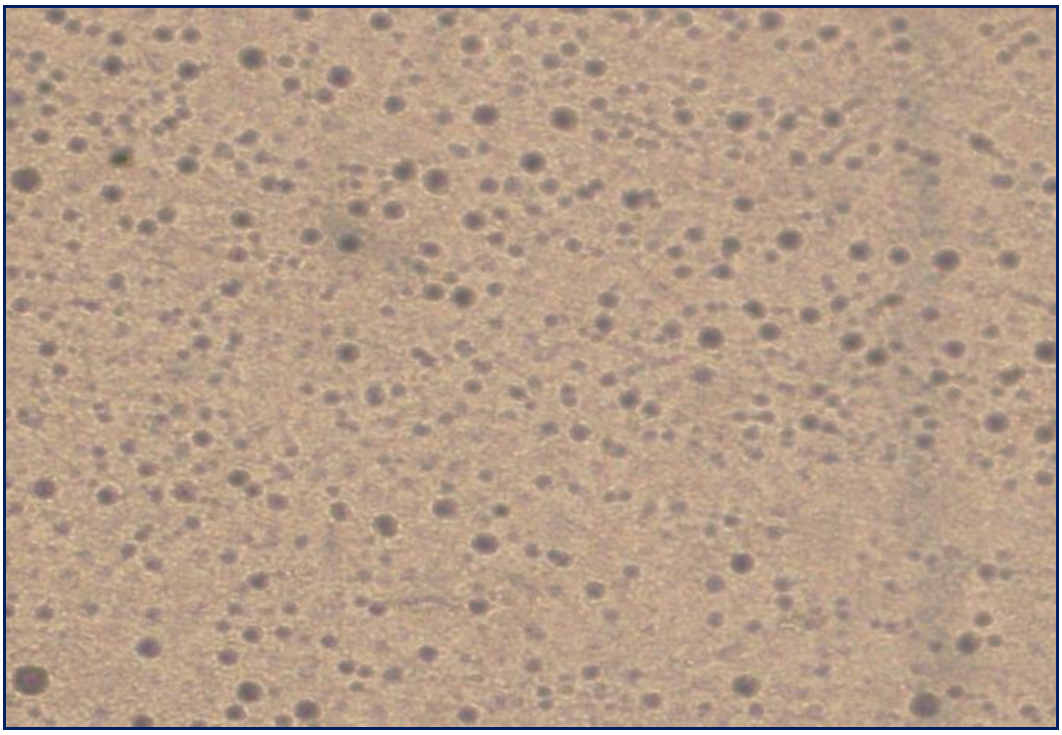

Figure 13. Trinocular image of ornidazole dental film.

Conclusion

The greatest advantage associated with the use of intra-pocket delivery systems over systemic delivery is that a less amount of drug is sufficient to achieve the effective concentration at the specific site. Application of antimicrobials into the local delivery system has been considered an important adjunct to conventional periodontal treatment. In the present study, periodontal films of ornidazole were prepared successfully using a hydrophobic polymer (polymer A) and a hydrophilic polymer (polymer B) in combination by simple solvent casting method.

From the present research we can conclude that:

- Periodontal films of ornidazole can be prepared by solvent casting method.
- Hydrophobic and hydroplilic polymer can be used as combination polymers to make periodontal films.
- The prepared ornidazole films can be used as antibacterial in different periodontal diseases.
- Further study on formulation optimization, compatibility, antimicrobial activity, stability and scale-up studies are needed to confirm the appropriateness of this formulated periodontal films.

References

Alam, M., Tasneem, F. and Pathan, M. S. I. 2014. Formulation and evaluation of swellable oral thin film of metoclopramide hydrochloride. *Bangladesh Pharm. J.* **17**, 102-112.

Aqther, A., Kumar, B. P. and Basha, P. 2013. Formulation and in-vitro evaluation of ornidazole gastroretentive tablets by using low density swellable polymers. *Ind. J. Res. Pharm. Biotechnol*. **1**, 597-601.

Armitage, G. C. 2004. Periodontal diagnoses and classification of periodontal diseases. *Periodontology* **34**, 9-21.

Ashwin, K., Saarangi, R., Ramesh, J., Sudhakar, B. and Reddy, P. 2013. Design and evaluation of biodegradable periodontal films containing ciprofloxacin and ornidazole. *Sch. Acad. J. Pharm*. **2**, 60-69.

Aviral, K., Prajapati, K., Ali, A. and Kumar, V. 2012. Formulation and evaluation of dental film for periodontitis. *Int. Res. J. Pharm*. **3**, 143-148.

Awen, B.Z., Katakam, P., Chandu, B.R., Adiki, S.K., Omar, S. and Mustafa, N. 2011. Subgingival films for controlled release of metronidazole using calcium alginate as drug retarding polymer: formulation and *in-vitro* evaluation. *Res Pharmaceutica* **2**, 1-9.

British Pharmacopoeia 2015. The British Pharmacopoeia Commission, London, UK.

Brunton, L.L., Chabner, B.A. and Knollman, B.C. 2011. Goodman & Gilman's Pharmacological Basis of Therapeutics, 12th edition.

Costa, P. and Lobo, J. M. S. 2001. Modelling and comparison of dissolution profiles. *Euro. J. Pharm. Sci*. **13**, 123-133.

Hasan, M. R., Hossen, M. A., Roy, A., Islam, T. and Pathan, M. S. I. 2014. Preparation of metformin hydrochloride extended release matrix tablets by direct compression method and its *in vitro* evaluation. *Brit. J. Pharm. Res*. **4**, 2679.

Mastiholimath, V.S., Dandagi, P.M., Gadad, A.P., Patil, M.B., Manvi, F.V. and Chandur, V.K. 2006. Formulation and evaluation of ornidazole dental implants for periodontitis. *Indian J. Pharm. Sci*. **68**, 68-71

Nair, S. C. and Anoop, K. R. 2012. Intraperiodontal pocket: An ideal route for local antimicrobial drug delivery. *J. Adv. Pharm. technol. res*. **3**, 9.

Prabhushankar, G.L., Gopal, K.B., Manjunatha, K.M. and Girisha, C.H. 2010. Formulation and evaluation of levofloxacin dental films for periodontitis. *Int. J. Pharm. Pharm. Sci*, **2**, 162-168.

Shankraiah, C. Nagesh, J. S., Venkatesh, M. and Lakshmi, N. 2011. Sustained release device containing ornidazole for periodontitis. *Int. Res. J. Pharm*. **2**, 217-221.

Sharma, N. and Gnanarajan, G. 2013. Recent trends in dental drug delivery systems. *Int. Res. J. Pharm*. **4**, 21-25.

Tasneem, F., Alam, M. and Pathan, M. S. I. 2015. Preparation and evaluation of metronidazole benzoate periodontal patches. *Bangladesh Pharm. J*. **18**, 97-102.

Vineetha, V. C. and Manju, M.M. 2015. Development and evaluation of dental films containing an antibacterial agent for the treatment of periodontitis. *Int. J. Pharm Pharm Sci*. **7**, 52-59.