Research Article

Comparison of Drug Release in Moxifloxacin in-SITU Gels by Franz and Open Ended Cell

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Accepted on: 13-05-2015; **Finalized on:** 30-06-2015.

ABSTRACT

This study reports the release properties of Moxifloxacin from in-situ gels measured with Open ended cylinder and Franz cell. For the two methods, a cellophane membrane previously soaked overnight in STF and dissolution mediums composed of Simulated tear fluid. Comparison of the release rates of Moxifloxacin from in-situ gel showed that the rate measured with the open ended cylinder was significantly slower than that measured with the Franz cell. The disadvantage of the Open ended cylinder was difficult operation and small sample sizes which caused variable results. The advantage of the Franz cell is better regression coefficients than Open ended cylinder. Franz cell is the more suitable apparatus for in-vitro drug release testing of Pharmaceutical semisolids preparations. This can be supported by the enhanced Flux and Permeation coefficient in Franz cell than Open ended cylinder. It was found that cumulative percent drug release was 80.756±4.437 and 73.03±1.321 for Franz cell and Open ended cylinder respectively after 8 hours. Flux, Permeation coefficients were 2.598±0.211, 5.269×10^{-4}±0.0000428 and 2.158±0.188, 4.337×10^{-4}±000038 for Franz cell and Open ended cylinder respectively.

Keywords: in-situ gels, Franz cell, cellophane membrane, semisolids.

INTRODUCTION

Historically, although *in vitro* release rate testing from semisolids could potentially provide valuable[1-3] information about product performance but it is not an industry wide quality control test requirement as compared to the utility of *in vitro* dissolution testing of oral dosage forms. To change this situation the extension of *in vitro* dissolution methodology to semisolid dosage forms has been the subject of substantial effort and debate. Similar to the dissolution testing of oral dosage forms, a simple, reliable and reproducible release rate method can guide formulation development; help to monitor batch-to-batch quality and stability, and control the manufacturing process of pharmaceuticals. This has led to the establishment of the FDA SUPAC-SS guidance requiring the performance of release testing from semisolid dosage forms after certain post approval changes. Although the FDA SUPAC-SS guidance include general methodology descriptions of diffusion systems, it does not specify a particular test methodology because currently no compendial *in vitro* release test methodology is described for semisolid dosage forms. Recently a significant amount of effort, research, innovation, and debate has surrounded the topic of *in vitro* dissolution methodology for semisolid dosage forms. From these reports, it is clear that a wide variety of diffusional systems[4-6] have been utilized and that the current dissolution testing systems for semisolid dosage forms originated from systems used for *in vitro* skin permeation studies. Among these methods, the Franz diffusion cell has been the standard system used for the study of semisolid drug formulations. First described by Franz in 1978, this cell has a small donor compartment and a cylindrical receptor chamber that allows mixing with a magnetic stir-bar[7-9]. This article reports the release properties of moxifloxacin from in-situ gels measured with the open ended cylinder and Franz cell.

MATERIALS AND METHODS

Corbopol 971P , HPMC K100, Tween 20 were purchased from Loba Chemie Pvt. Ltd., Mumbai. Sodium hydroxide, and Benzalkonium chloride were purchased from S.D Fine chemicals Ltd., Mumbai.

Preparation of in-situ gel

Composition of in-situ gel was given in **Table1** with required quantities of all ingredients. Corbopol and HPMC K100 were sprinkled over 75 mL of distilled water and allowed to hydrate overnight. Add the required amount of Sodium hydroxide.

Table 1: Composition of in-situ gel

S No	Ingredients	Quantity (%w/v)
1	Moxifloxacin	0.5
2	Corbopol 971P	0.35
3	HPMC K100	0.75
4	Tween 20	1
5	Benzolkonium Chloride	0.01
6	Sodium Hydroxide	0.16
7	Distilled Water (q. s to)	100ml

After forming clear solution Tween20 was added to the polymer solution with stirring. Moxifloxacin was dissolved in 25 mL of distilled water separately. Add benzolkonium chloride to the above drug solution. Then filter the

solution through 0.2µ Cellulose acetate membrane to avoid particulate matter. Then add the drug solution to polymer solution under constant stirring until a uniform solution was obtained then adjust the final volume to 100 mL with distilled water and subjected to terminal sterilization by autoclaving at 121ºC and 15 lb for 20 min.

In vitro Release Studies

Open Ended Cylinder

The dissolution medium used was artificial tear fluid freshly prepared (pH 7.4). Cellophane membrane, previously soaked overnight in the dissolution medium, was tied to one end of a specifically designed glass cylinder (open at both ends and of 2 cm diameter). A 1mL volume of the formulation was accurately pipetted into this assembly. The cylinder was attached to the metallic driveshaft and suspended in 200 mL of dissolution medium maintained at 37± 1°C so that the membrane just touched the receptor medium surface. The dissolution medium was stirred at 50 rpm using magnetic stirrer. Aliquots, each of 5-mL volume, were withdrawn at hourly intervals and replaced by an equal volume of the receptor medium. The aliquots were diluted with the receptor medium and analyzed by UV-Vis spectrophotometer at 288 nm.

Franz cell

The dissolution medium used was artificial tear fluid freshly prepared (pH 7.4). Cellophane membrane, previously soaked overnight in the dissolution medium, was placed on receptor compartment. Receptor compartment was filled with 14mL of dissolution medium and was maintained at 37± 1°C. Care should be taken such that the membrane just touched the receptor medium surface. A 150µL volume of the formulation was accurately pipetted into donor compartment. The dissolution medium was stirred at 50 rpm using magnetic stirrer.

Aliquots, each of 2-mL volume, were withdrawn at hourly intervals and replaced by an equal volume of the receptor medium. Care should be taken while sampling without forming air bubbles in the receptor compartment. The aliquots were diluted with the receptor medium and analyzed by Double beam UV-Vis spectrophotometer at 288 nm.

RESULTS AND DISCUSSION

In-vitro drug release study of the in-situ gel was performed in Open ended cylinder and Franz diffusion cell. It was found that cumulative percent drug release was 80.756±4.437 and 73.03±1.321 for Franz cell and Open ended cylinder respectively after 8 hours is shown in **Table 2**. Flux, Permeation coefficients were 2.598±0.211, 5.269×10^{-4}±0.0000428 and 2.158±0.188, 4.337×10^{-4}±000038 for Franz cell and Open ended cylinder respectively. At initial time points (15, 30 and 60min) the Cumulative percent drug release was more in Open ended cylinder, this may be because of presence of high concentration gradient than Franz cell due to the presence of large volume of dissolution medium in Open ended cylinder that is 200mL, where as in Franz cell it is only 14mL. After 60min Cumulative percent drug released was slightly enhanced in Franz cell compared to Open ended cylinder. This can be supported by the enhanced Permeation coefficient in franz cell than Open ended cylinder. This may be because of the inefficient mixing of the dissolution medium during the test that means the magnet was present at bottom of the beaker in Open ended cylinder. But in Franz cell the receptor compartment was small and efficient mixing of the dissolution medium is possible. The results obtained were fit into various plots of Zero order, First order, Higuchi matrix and Peppas models is shown in **Table 3**. From the results, it is clear that the drug release in Franz cell showed better regression coefficients than drug release in Open ended cylinder, because chance of experimental errors are more in Open ended cylinder that's why data from Open ended cylinder had more fluctuations compared to Franz cell data is shown in **Table 4**. Form this we can say experimental errors were minimized by using Franz diffusion cell is shown in **Figure 1**. That's the reason why US FDA approved Franz cell for *in-vitro* diffusion study of semisolid preparations.

Table 2: comparison of release kinetics of Moxifloxacin in Franz cell and Open ended cylinder

Time (min)	% Cum Released		Log % Released		Log % Un Released	
	Franz Cell	Open ended Cylinder	Franz Cell	Open ended Cylinder	Franz Cell	Open ended Cylinder
15	8.753 ± 0.205	11.425 ± 2.892	0.951	1.058	1.960	1.947
30	12.331 ± 0.751	14.536 ± 1.354	1.127	1.162	1.943	1.932
60	17.325 ± 0.812	19.721 ± 3.802	1.267	1.295	1.917	1.905
120	27.254 ± 1.158	25.622 ± 2.374	1.461	1.409	1.862	1.871
180	36.340 ± 1.823	34.296 ± 2.136	1.590	1.535	1.804	1.818
240	44.250 ± 2.497	43.161 ± 4.574	1.679	1.635	1.746	1.755
300	51.454 ± 2.825	52.496 ± 3.468	1.744	1.720	1.686	1.677
360	58.702 ± 3.331	61.878 ± 2.126	1.802	1.792	1.616	1.581
420	65.864 ± 3.945	69.388 ± 2.350	1.854	1.841	1.533	1.486
480	80.756 ± 4.437	73.037 ± 1.323	1.887	1.864	1.466	1.431

Table 3: Model fitting of release of Moxifloxacin in Franz cell and Open ended cylinder

Instrument	Zero Order	First Order	Higuchi-Matrix	Karsmayer-Peppas		Best fit model
	R^2	R^2	R^2	Slope (n)	R^2	
Franz Cell	0.992	0.989	0.981	0.629	0.995	Peppas
Open ended cylinder	0.995	0.972	0.952	0.553	0.972	Zero

Table 4: comparison of Permeation kinetics of Moxifloxacin in Franz cell and Open ended cylinder (n=3, error bars represent standard error)

Instrument	Flux (J) $\mu gm/cm^2.min$	Permeation Coefficient (P) $Cm/min \times 10^{-4}$
Franz Cell	2.598 ± 0.211	5.269×10^{-4} ± 0.0000428
Open ended cylinder	2.158 ± 0.188	4.377×10^{-4} ± 0.0000380

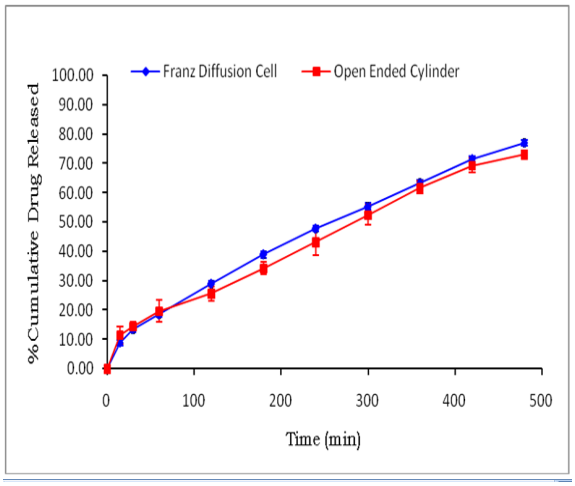

Figure1: Comparative release of Moxifloxacin in Franz cell and open ended cylinder (n=3, error bars represent standard error)

CONCLUSION

The results presented also showed that the Franz cell and Open ended cylinder can be used for these purposes to test pharmaceutical semisolid preparations if appropriate dissolution medium and membrane are used. The main advantages of the Franz cell over the Open ended cylinder are the ease of operation and minimum experimental errors ensuring more consistent results. Although the Franz cell and Open ended cylinder gave similar release results for the products tested in this study, the advantage of the Franz cell is better regression coefficients than Open ended cylinder. Franz cell is the more suitable apparatus for *in-vitro* drug release testing of Pharmaceutical semisolids preparations. This can be supported by the enhanced Flux and Permeation coefficient in Franz cell than Open ended cylinder.

Acknowledgement: The authors are very much thankful to Management and principal of KVSR Siddhartha College of pharmaceutical sciences, Vijayawada for their support and constant encouragement.

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Source of Support: Nil, **Conflict of Interest:** None.