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Erosion-diffusion cell: a new apparatus to study in-vitro drug release from erosion-diffusion based formulations

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Abstract

Erosion-diffusion (E-D) cell has been designed to study in vitro drug release from a variety of dosage forms like tablets, capsules, pellets, powders, films, patches, granules, micro-spheres, micro-capsules etc. It provides a better and effective alternative as compared to USP XXVI dissolution rate test apparatus.

It consists of central body region, outer body region, screen, cap, sampling port and lid. Design and handling of E-D cell is better as compared to USP Dissolution rate test apparatus. Equipment is evaluated on the basis of sensitiveness, effectiveness and easiness to determine in vitro drug release, degree of stirring and quality of glass used. Apart from this, separate dissolution study was performed and the profile was compared with USP XXVI dissolution rate test apparatus.

Test for hydrolytic resistance or limit of alkalinity (Crushed-glass test USP) indicated that the type of glass used for designing E-D cell was type I glass. $KMnO_4$ mauve stirring test suggested that E-D cell coupled with magnetic stirrer could provide instantaneous and acceptable stirring required during dissolution studies. The profile obtained by E-D cell was better in terms of release order.

Key words: Erosion, diffusion, erosion cell, diffusion cell, *in vitro* drug release, mauve sirring test.

Introduction

In dosage form design, the in-vitro drug release studies constitute a major role among all other aspects of the research. A lot of research has been oriented for the development of in-vitro evaluation techniques for novel drug delivery systems. However, no serious consideration has been given for the development of any new apparatus to study in-vitro drug release especially from erosion-diffusion based formulations. The traditional USP dissolution rate test apparatus is being used wherever in-vitro drug release studies for these types of systems are needed (Das et al. 2000, Takka and Acarturk 1999, Stephan et al. 2007, Maeda et al. 2004, Zimmerman et al. 2004, Shun et al. 1995, Wakerly et al. 1996). This paper aims at the development of E-D cell that can be used effectively for these formulations. Design and handling of E-D cell is novel as compared to USP Dissolution rate test apparatus due to compactness and miniature form, less cost, easy sampling and replenishing of dissolution media, less quantity of the dosage form and dissolution media required and easy cleaning by de-assembling the cap and body regions. Equipment is evaluated on the basis of sensitiveness, effectiveness and easiness to determine in vitro drug release, degree of stirring and quality of glass used.

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In vitro drug release pattern using this equipment was compared with that of USP XXVI dissolution rate test apparatus.

Materials and Methods

Materials

Borosilicate glass, Stainless-steel screen and Magnetic stirrer were purchased from Atul Chemicals and Scientific Works, Ambala Cantt. (India).

Methods

Design and handling of E-D cell: E-D cell consists of following parts as shown in Figure 1:

Zone I:	Central body region (Internal diameter: 30mm, Height: 35mm)
Zone II:	Outer body region (Internal diameter: 70mm, Height: 45mm)
Zone III:	Screen (Internal diameter: 68mm)
Zone IV:	Cap (Internal diameter: 71mm, Height: 43mm)
Zone V:	Sampling port (Internal diameter: 20mm, Height: 43mm)
Zone VI:	Lid (Internal diameter: 30mm)

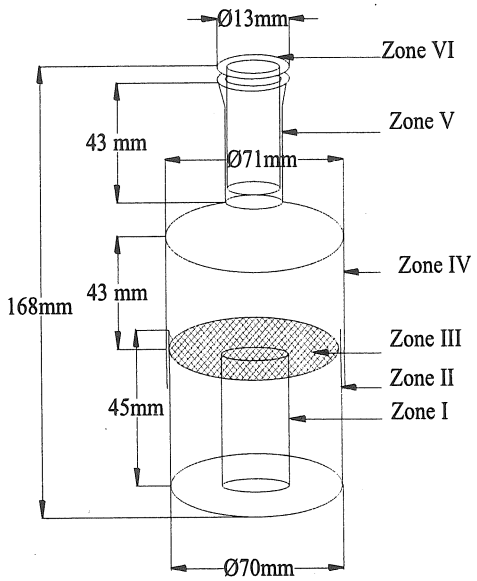

Fig: Three Dimensional View of the Erosion Diffusion Cell

(ZoneI: Inner Body Region; Zone II: Outer body Region; Zone III Screen; Zone IV Cap; Zone V: Sampling Port; Zone VI: Lid)

Figure 1. Three dimensional view of erosion-diffusion cell

Lower part of the body is divided into central and outer regions. The outer region supports a detachable screen made of stainless steel. All other parts of the cell are made of borosilicate glass. The body is covered by a cap that contains a sampling port at the top. Sampling port can be opened and closed by means of a lid.

The dosage form whose release study is to be performed is placed in outer region of the body and screen is placed above the body as shown in the figure. Dissolution medium is added, the cap is fitted on to the body and lid is closed. The cell is placed on a magnetic stirrer, which is adjusted to the desired level of

stirring and temperature. After specified time intervals, a predetermined quantity of sample can be removed from the central body region through the sampling port and same quantity of dissolution media can be replenished so that volume remains constant.

Test for hydrolytic resistance or limit of alkalinity (Crushed-glass test USP): From the glass containers, alkaline constituents (oxides of sodium, potassium calcium aluminum etc.) are leached into purified water under condition of elevated temperatures. When the glass is powdered, the leaching of alkali can be enhanced. The amount of alkali leached is critical.

One of the E-D cell was rinsed thoroughly with purified water and dried with a stream of clean and dry air. The cell was taken into a mortar and ground to a fine powder using a pestle. The glass powder was passed through 20 – mesh sieve placed over 50 – mesh sieve. The glass powder that was retained on 50 - mesh sieve was collected and used for the test. The specimen (10.0g) was transferred into a 250 ml conical flask and washed with about 30.0 ml acetone. Washing was repeated with acetone and acetone was carefully decanted.

The powdered and washed glass powder specimen (10.0g) was accurately weighed and transferred into a 250 ml conical flask. 50 ml of high purity water was added to this flask. The flask was capped and autoclaved at 121±2°C for 30minutes. Then solution was decanted into another conical flask. The residual powder was washed with 15 ml portions of high purity water. Again aliquot is decanted into the conical flask (main portions). The total volume was made up to 100 ml. About 5 drops of methyl red solution was added and titrated immediately with 0.02 N sulfuric acid solutions. End point was yellow to red. The volume of 0.02 N sulfuric acid solution consumed was recorded. The volume should not exceed the limit that indicated for the type of glass container (Table 1).

Table 1. USP limit for crushed glass test

Test	Containers	Limits, ml of 0.02 N H_2SO_4
Powdered glass test	Type I	1.0
	Type II	8.5
	Type NP	15.0

$KMnO_4$ mauve stirring test: Instantaneous stirring was performed according to G.C.L. Gummer et al., method. E-D cell accommodated a crystal of $KMnO_4$ and a stirring bar. The cell was stirred at around 600 revolutions per minute for 2 minutes using magnetic stirrer. The degree of dispersal mauve coloration from the permanganate crystal was used to qualitatively access the degree of stirring. In this method, complete and even coloration within 30 seconds is considered as instantaneous and acceptable stirring (Gummer et al. 1987).

In vitro drug release study: For these studies, acetyl salicylic acid (ASA) was used as a model drug and the release of ASA from directly compressed alginate tablets was investigated.

Preparation of tablets: Matrix tablets (400 mg) were prepared by direct compression method, using following composition:

Acetyl salicylic acid (ASA)	100 mg
$CaHPO_4.2H_2O$	50 mg
$Na_3PO_4.12H_2O$	60 mg
MCC PH 102	90 mg
Alginate (Protanal LF 120M, Viscosity 103 mPa)	100 mg

All the ingredients were mixed, and the powder mixtures were compressed into tablets using single punch tablet making machine.

Tablet characterization: The tablets were characterized immediately after preparation. The tablets diameter and thickness were measured using vernier caliper. The tensile strength of the tablets was measured using Erweka HBT 28 crushing strength tester.

Drug release studies: Drug release from tablet formulations was assessed using E-D cell and USP XXVI dissolution rate test II (Paddle) apparatus. The dissolution medium was 0.1 M HCl for initial 2 hours and then dissolution was continued using Phosphate buffer pH 6.8. The temperature of the release medium was kept at 37^0C. Samples were withdrawn from the vessel every 10 minutes, and released ASA was determined spectrophotometrically. Absorbances were compared with that of a standard curve and the amount of ASA released was calculated.

Results and Discussion

Design and Handling of E-D cell: The E-D cell can be easily handled due to its miniature form and can be easily de-assembled for cleaning purposes. It is cheap and effective alternative as compared to USP Dissolution rate test apparatus. Design and handling of E-D cell is better as compared to USP Dissolution rate test apparatus due to following reasons:

a) The equipment is compact and in miniature form.

b) Cost is very low as compared to USP Dissolution rate test apparatus.

c) Sampling and replenishing is very easy.

d) Less quantity of the dosage form and dissolution media is required for in-vitro drug release studies.

e) Equipment can be easily handled and easily carried from one place to another, if required.

f) Whole of the equipment can be easily cleaned by de-assembling the cap and body regions.

g) It is especially useful in case of in-vitro drug release testing of pellets, powders, films, patches, granules, micro-spheres, microcapsules etc.

Test for hydrolytic resistance or limit of alkalinity (Crushed-glass test USP): In test for hydrolytic resistance or limit of alkalinity (Crushed-glass test USP), the volume of 0.02 N sulfuric acid solution consumed was 0.8 ml, which was under the limit specified for type I (Highly resistant borosilicate) glass. As the volume of 0.02 N sulfuric acid consumed was under the limit specified for type I (Highly resistant borosilicate) glass, so, the type of glass used for designing E-D cell was type I glass.

$KMnO_4$ mauve stirring test: $KMnO_4$ mauve stirring test was performed to check the degree of dispersal mauve coloration from the permanganate crystal within E-D cell. It was noted that complete and even coloration was obtained in 07 seconds. So, results suggested that E-D cell coupled with magnetic stirrer could provide instantaneous and acceptable stirring required during dissolution studies.

Tablet characterization: The tablets were characterized for their diameter, thickness and tensile strength. All tablets had a diameter of 10 mm. The tablet thickness was found to be 3.73 mm. Tensile strength of the tablets was found to be 1.6±0.3.

Drug release studies: The amount of ASA released from tablet formulations using E-D cell and USP XXVI dissolution rate test II (Paddle) apparatus was plotted against time (Figure 2). The present study suggested that the in-vitro profile obtained by E-D cell is nearly zero order as compared to that of USP XXVI dissolution rate test II (Paddle) apparatus.

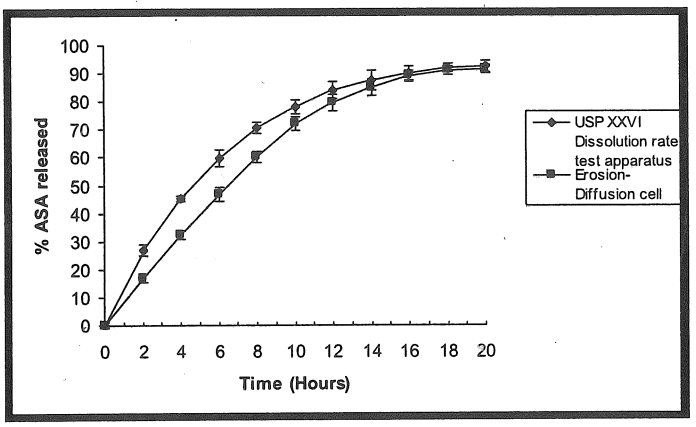

Figure 2. % ASA released vs. time

Conclusion

The present study suggests the need of a novel apparatus to study in-vitro drug release from a variety of dosage forms. Design of E-D cell is one such step in this direction that aims at easiness, compactness and effectiveness of the in-vitro drug release apparatus. Design and handling of E-D cell is better as compared to USP Dissolution rate test apparatus. Test for hydrolytic resistance or limit of alkalinity (Crushed-glass test USP) indicated that the type of glass used for designing E-D cell was type I glass. $KMnO_4$ mauve stirring test suggested that E-D cell coupled with magnetic stirrer could provide instantaneous and acceptable stirring required during dissolution studies. Drug release studies of prepared matrix tablets suggested that the in-vitro profile obtained by E-D cell is nearly zero order as compared to that of USP XXVI dissolution rate test II (Paddle) apparatus. So, it can be concluded from this study that E-D cell provides a better and effective alternative as compared to USP Dissolution rate test apparatus.

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