DEVELOPMENT OF COMPUTER CONTROLLED IONTOPHORETIC DRUG DELIVERY SYSTEM

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Date: 30.05.2013

This is to certify that the thesis entitled "**Development of computer controlled iontophoretic drug delivery system**" submitted by **Mr. Uttam kumar** in partial fulfillment of the requirements for the award of Master of Technology Degree in **"Biomedical engineering"** at the National Institute of Technology, Rourkela, Odisha is an authentic work carried out by him under my supervision and guidance. To the best of my knowledge, the matter embodied in the thesis has not been submitted to any other University / Institute for the award of any Degree or Diploma.

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In the end I must record my special appreciation to my almighty who has always been source of my strength, inspiration and my achievements.

Date: ***Uttam kumar***

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ABBREVIATIONS

Abbreviation	Definitions
CCS	Constant current source
WG	Waveform generator
SSC	Signal conditioning circuit
SA	sodium salicylate
CPDR	Cumulative percent drug release
DW	Distilled Water
w/w	Weight by Weight
w/v	Weight by Volume
SS	Stainless Steel
µm	Micrometer
R^2	Regression coefficients
OD	Optical Density
SO	Sunflower oil
SM	Surfactant mixture
Rb	Bulk resistance
HW	Half wave rectifier
FW	Full wave rectifier
TR	Triangular waveform
PD	Pulse DC
PAS	Passive
SN	Sinusoidal wave
SQ	Square wave
TR	Triangular
SQH	Square of half wave
SNH	Sinusoidal of half wave
SNF	Sinusoidal of full wave

Abstract

In this study, attempts were made to develop computer controlled iontophoretic drug delivery system. The iontophoretic set up was made using NI SPEEDY33 voltage buffer, constant current source and specially designed diffusion cell. The stability of constant current source was checked by varying the load resistance and measured the voltage across it. Different wave forms were generated using NI SPEEDY 33 and LABVIEW 8.6 and they were employed in the *in vitro* drug delivery. The effectiveness of iontophoretic set up was tested using span 80-tween 80 based sunflower oil organogels. The organogels were characterized using SEM, FTIR and XRD studies. Thermal, textural, visco-elastic and electrochemical properties of the organogels were also studied. The in vitro drug release studies were performed using different wave forms viz., sinusoidal waveform ,square waveform and triangular waveform. and also the half wave and full wave of sine waveform . The active drug release from the gels was compared against passive diffusion. The drug release followed the zero order kinetics suggesting the diffusion mediated release. The Krossmeyer-Peppas kinetics suggested the anomalous release of drugs during active diffusion of drugs. The results suggest that the developed iontophoretic set up has a huge potential in the iontophoretic drug delivery system.

Keywords: NI SPEEDY 33 , LABVIEW 8.6 , iontophoresis, organogels

Chapter 1

Introduction and objective

1 Introduction

Skin is the largest organ and the integumentary system of the body [1]. It has been explored to deliver drugs either to elicit pharmacological actions locally or systemically [2]. The delivery of drugs into the systemic circulation across the skin is regarded as transdermal delivery. The main advantage of transdermal drug delivery is by passing the first pass metabolism by the drug molecules. But the migration of drug from the skin surface into the systemic circulation is the rate-limiting step. Many approaches (e.g. use of permeation enhancers, electrical energy, ultrasound or a combination of these) have been adopted to improve the permeation of the drugs through the skin layer [2]. Amongst the techniques studied, iontophoretic drug delivery system has evolved as one of the widely studied transdermal drug delivery systems. Iontophoresis is a non-invasive transdermal drug delivery methodology which uses a low intensity electric current to promote permeation of the drug across the skin[3]. The method is based on the phenomenon of *like charges repel each other*. The technique uses a two electrode system. One of the electrodes is the active electrode while the other is the passive electrode. The drug molecules used for iontophoretic drug delivery are usually charged molecules. But various neutral drug molecules have also been tried. If the drug molecules are anionic in nature then cathode is made the active electrode and vice versa. The delivery of the drug has been found to be dependent on the profile of the electric current applied. Various current profiles have been applied and their effect on the release profile has been studied extensively.

Drugs are usually incorporated within gel based matrices. The drug loaded matrices are placed in the donor compartment. The matrices should be electrically conductive in nature. Till recent past, only hydrogels were regarded as suitable for iontophoretic delivery systems. Hydrogels are polymeric matrices which can imbibe and hold water within the polymeric structures. Of late, water containing organogels have also been tried as drug delivery matrices for iontophoretic drug delivery systems. Organogels are gel based systems which immobilizes apolar solvents. In general, organogels are electrically non-conductive. Organogel based formulations may be designed to contain pockets of water, which can make the organogels electrically conductive. The development of organogels is much easier as compared to the hydrogels. Organogel based delivery systems have shown good potential to be used in iontophoretic drug delivery systems.

The current study deals with the development of a computer controlled iontophoretic drug delivery system. In our previous study, we have reported development of span 80- tween 80

based organogels. Three compositions of organogels were chosen and were analyzed for their ability to act as matrices for iontophoretic drug delivery.

1.2. Objective

Development of computer controlled iontophoretic drug delivery system.

Chapter 2

Literature review

2.1. Iontophoretic drug delivery

Iontophoresis is a technique to deliver the drug or other chemical through the skin with the help of small electric charge [4]. It is important because of without injection of needle. This process is also called a non invasive method of propelling high concentrations of charged substances. The non invasive nature of the method has led to the increase in the patient compliance. Iontophoresis is well classified for use in transdermal drug delivery with more recent investigations focusing on applications such as sweat testing for the diagnosis of cystic fibrosis, hyperhidrosis, local anesthesia, and for ulcers. Additionally, over the last few decades, iontophoresis has come to be used as a technique researched primarily for its use in the delivery of charged ions and macromolecules through the skin for systemic circulation [5]. iontophoresis provides a non-invasive method for the delivery of agent at therapeutically significant level due to its enhancement effect on skin permeation. These benefits are specially significant for administration of protein and peptides which do not achieve therapeutically significant concentrations by the oral delivery route. This technique allows the effective delivery of drugs with short biological half lives, as it shortens the time frame from administration to delivery the target tissue. Patient compliance is significantly improve due to infrequent dosing, and treatment can be terminated when needed. The advantage of this technique are accompanied by limitation of procedure, the most obvious being the potential for burning and pain on application of electric current. This technique is considered safe, if increasing the intensity of the applied electric charge can be led to irritation, burning , necrosis and erythema etc. an iontophoresis is usually restricted to compounds that can be formulated in their ionic form. In case of ionic compound, the pH of the skin is not the same in deeper layer as it is at the surface. This may lead to ineffective iontophoresis for some molecules due the effect of pH on ionization. Here this phenomenon related with proteins and peptides where the charge is an important factor in their delivery and stability. The effective iontophoretic transport of charged species may also be affected by an ion competition factor due to the presence of other moieties and also the degradation or adsorption of the drug under the electrode.

2.2. Operational amplifier

IC OP07 is an op amp which is used for both inverting and non-inverting amplification and for many more applications such as constant current source, voltage buffer, current mirror etc. gain (AV) in non inverting mode = 1+ (R2 / R1) and inverting mode = (-R2/R1) [6]. Pin configuration has been given in figure 1.

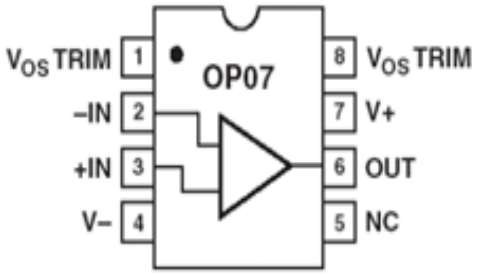


Figure 1: Pin configuration of OP07

2.3. NI SPPEEDY 33

The SPEEDY-33 is an educational Digital Signal Processing development board that is easily programmed using the LABVIEW DSP Module [7]. SPEEDY33 stands for signal processing educational engineering device for youth. The number 33 comes from the DSP chip TMS320VC33 made by Texas Instruments. The TMS320VC33 operates at 150MHz. here we are using SPEEDY-33 as a waveform generator. The figure of SPEEDY 33 has been given below.

Figure 2: SPEEDY 33

2.4. Constant current source

The constant current source is circuit which sinks or sources a constant current regardless of changing load resistance or power supply voltage [8]. The constant current source is needed to

supply invariant current with varying load, temperature and input voltage. the constant current source is used for impedance measurement, converts the sinusoidal voltage to current which is unaffected by load [9]. There are different techniques for implementing the voltage controlled voltage source (VCCS) for measuring bioimpedance: VCCS using an inverting amplifier, transformer coupled op amp, Howland configuration of op amp, current mirror based current source.

2.5. VCCS using an inverting amplifier

The voltage controlled current source (VCCS) using single op amp inverting amplifier is the simplest method to implement. In this method, the load resistance is connected to the feedback path of the amplifier. This constant current source can be used in the delivery of the drug into the body [10].

2.6. Howland constant current source

The Howland constant current source is a current source which is used to implement differential current source. This type of current source is implemented connecting two current sources in series [11].

In this type of current source balance should be maintained to between the two current sources. If any imbalance of parameter occurs in the current sources of Howland current source, it may cause a non-nominal value of current injected through the sample and common mode signal.

2.7. Current mirror based constant current source

Current mirror based constant current source is more advantageous than the other type of VCCS as it has high output impedance. It consists of a current generator, a current mirror and a current regulator [12]. Current mirror circuit with high precision has highly accurate current ratio and it prevents variation of output voltage due to its high output impedance.

2.8. Rectifier

Rectifier is an electrical device that converts alternating current to direct current. It is only one directional flows. This process is called rectification. Present day it take a number of forms including solid state diode, SCR and other silicon based semiconductor switches.

2.8.1. Half wave rectifier

In the half wave rectification circuit either positive or negative half of AC wave is passed, while the other half is blocked. It depends only on diode conditions. It can be used to obtain the desired value of dc voltage it has also provides a isolation from the power line [13]. The half wave circuit diagram shown in figure 3.

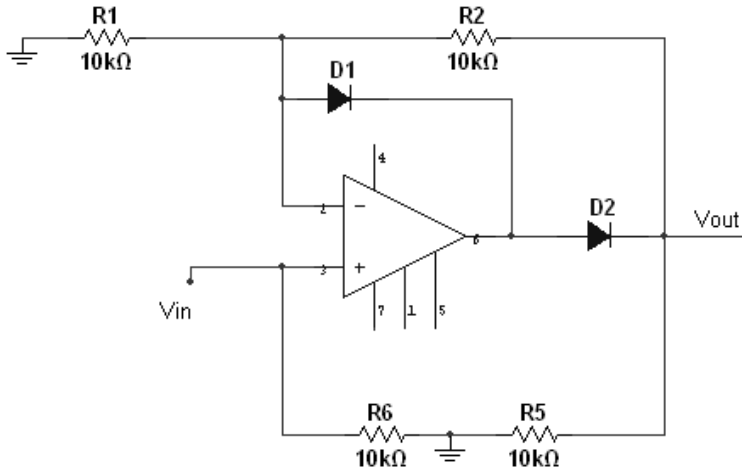


Figure 3: Circuit diagram of half wave rectifier

2.8.2. Full wave rectifier

The full wave rectifier circuit converts the whole of the input wave form to one of constant polarity as its output. Full-wave rectifier circuit converts both polarities of the input waveform to DC and yields a higher mean output voltage [14]. The circuit diagram of full wave rectifier shown in figure 4.

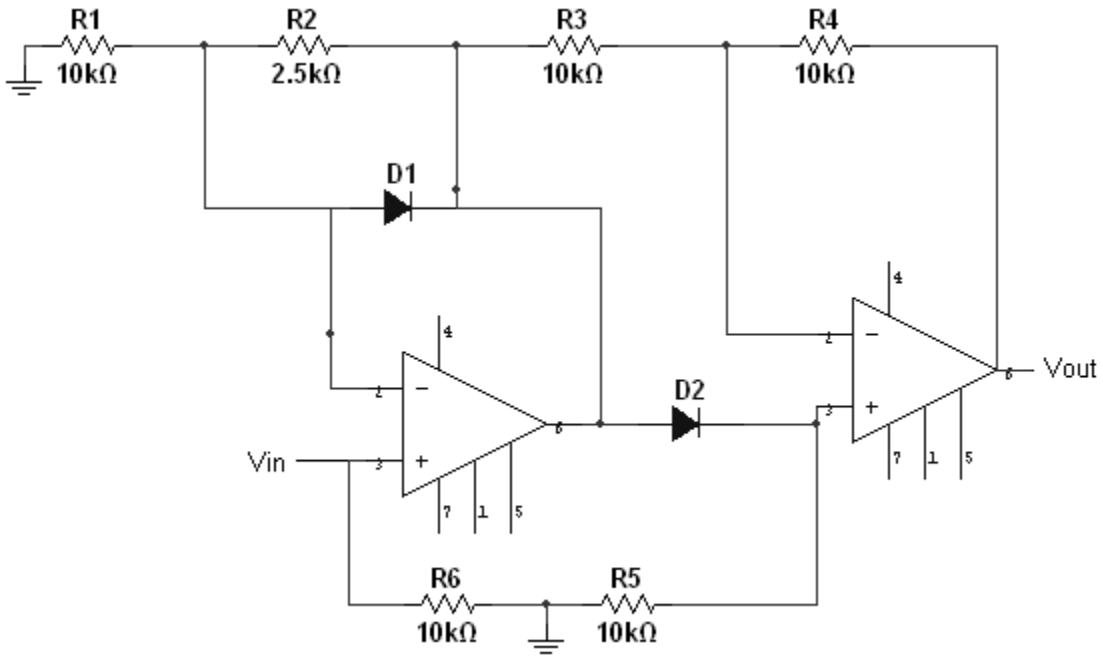


Figure 4: Circuit diagram of full wave rectifier

2.9. Organogels

Gel is nothing but it is colloid suspension of solid particles. It is a semisolid system, by the three dimensional (self-assembled, intertwined gelator fibers) network the liquid phase is immobilized, despite the majority of liquid composition it demonstrate the appearance and rheological behaviour of solids. In last few decades Investigative research pertaining to these systems [15]. A various application of the organogels such as drug delivery mediums for topical and oral pharmaceuticals, organic application medium for cosmetics, cleaning material for art conservation, delivery nutrient or neutraceuticals (vitamins and supplements), particale in personal core product (shampoo, conditioner), crystalline fat in food processing etc.

Chapter 3

Materials and methods

3.1. Materials

IC OP07 was procured from Analog Devices, Noorwood, USA. SPEEDY 33 was procured from National instruments, USA. Other basic electronic components were procured from the local market. Span 80 (sorbitan monooleate; SM) was purchased from Loba Chemie, Mumbai, India. Tween 80 (polyoxyethylene sorbitan monooleate; PM) and Sodium salicylate (SA) were purchased from Hi-media, Mumbai, India. The stainless steel (SS) electrodes for the iontophoretic studies were fabricated from the high quality SS plates procured from the local market. Edible grade refined sunflower oil (SO) was procured from the local market. All the studies were conducted using double distilled water (DW).

3.2. Circuit development

The basic waveforms (e.g. sine, triangular and square) were generated using computer controlled SPEEDY-33. The output from the SPEEDY-33 was connected to a voltage buffer (to protect the SPEEDY-33) followed by a signal conditioning circuit (SCC) to modulate the basic waveforms as desired. The SCC was avoided if the basic waveform was to be used. The setup of computer-SPEEDY-33-SCC acted as a waveform generator (WG). The output of the WG was connected to an OPAMP based voltage-controlled constant current source (CCS) working in the inverting amplification mode. The CCS was connected with the 2 electrode system. Depending on the polarity of the electrodes, one of the electrodes served as the active electrode while the other electrode was used as the passive electrode. These electrodes were connected to the specially designed diffusion cell, which contained a drug reservoir, a receptor and a dummy reservoir (Figure 5). The schematic diagram of the complete setup has been shown in (figure 6)

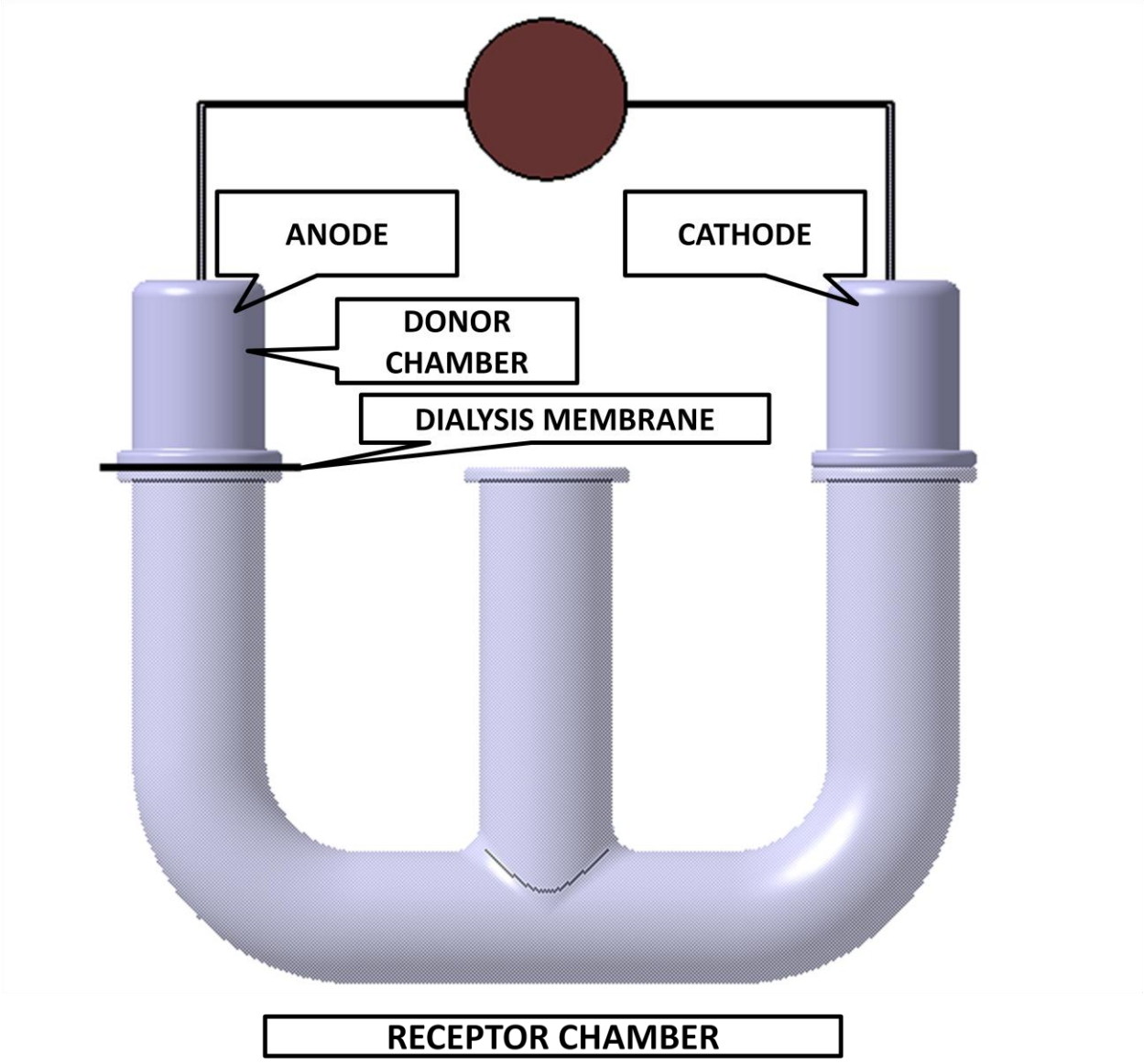


Figure 5: Block diagram of the Franz diffusion cell

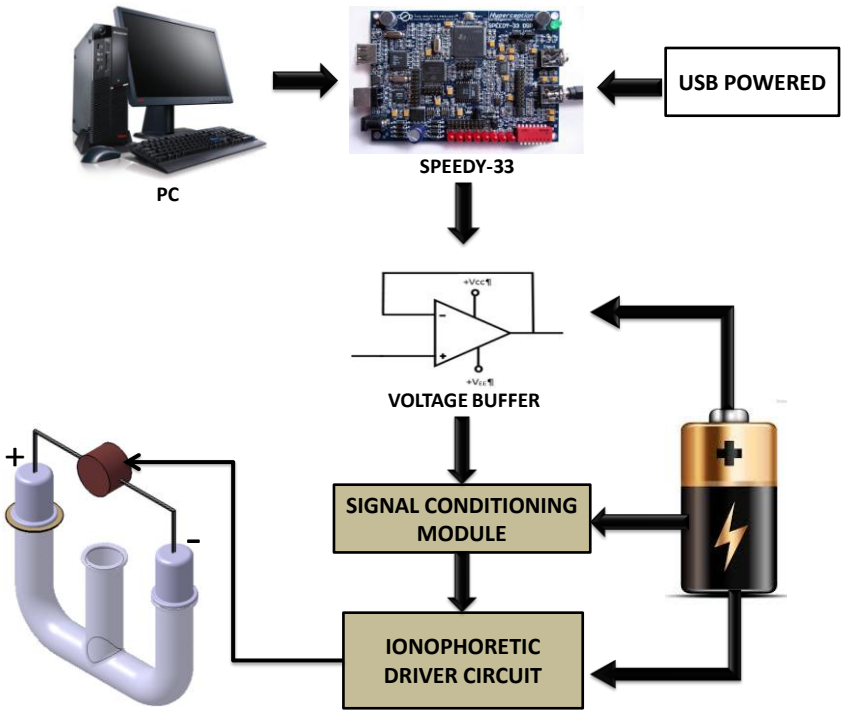


Figure 6: Block diagram of iontophoretic drug delivery system

3.3 Signal conditioning circuit (SCC)

The basic waveform signals from the voltage buffer were fed into the SCC. The SCC was either precision half-wave rectifier or precision full-wave rectifier. The SCC has been designed as per the previously reported literature. The circuit diagrams of the SCCs have been shown in figures 7 and 8. The proper functioning of the SCCs was tested by applying the basic waveforms into the SCCs and monitoring the output of the SCCs.

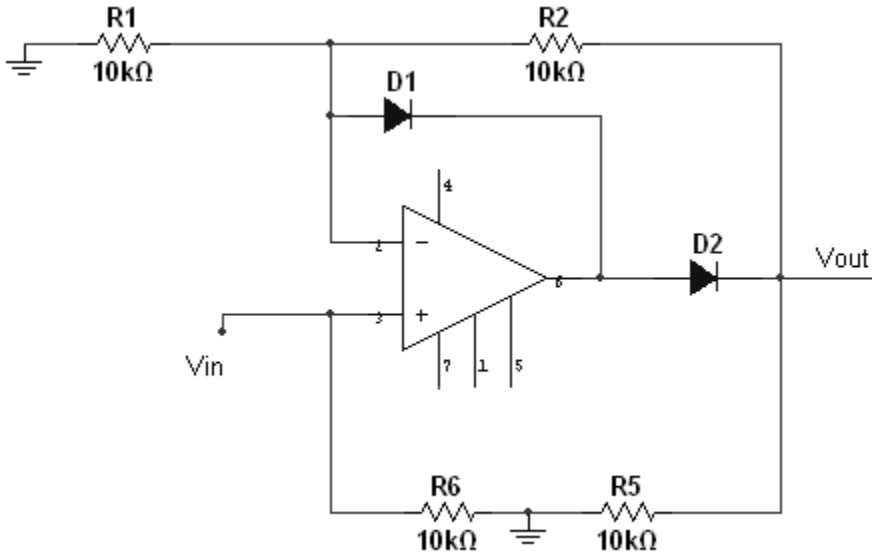


Figure 7: Circuit diagram of half wave rectifier

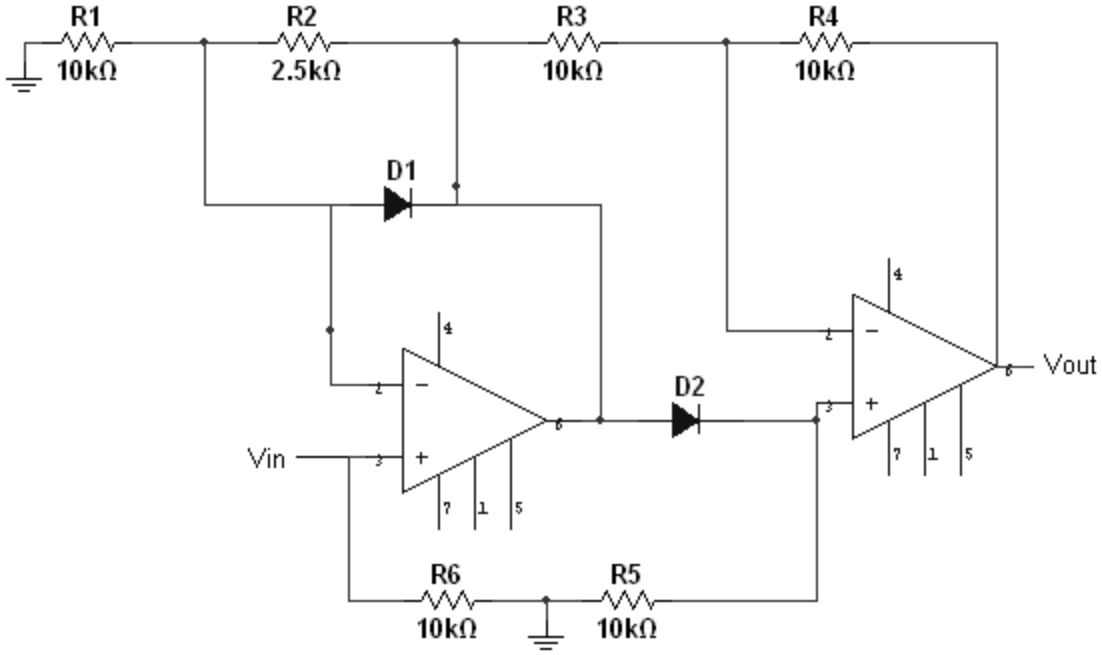


Figure 8: Circuit diagram of full wave rectifier

3.4. Designing of Constant current source circuit (CCS)

CCS was designed using IC OP07 working in the inverting amplifier mode (figure 9). The output of the voltage buffer was fed into the inverting terminal of the IC OP07 through a variable resistance (R_1: 10 KΩ). R1 was chosen from the previously conducted impedance measurement studies. The stability of the CCS was studied by varying the load resistance and measured the

output voltage across it. The circuit diagram of constant current source has been shown in figure 9.

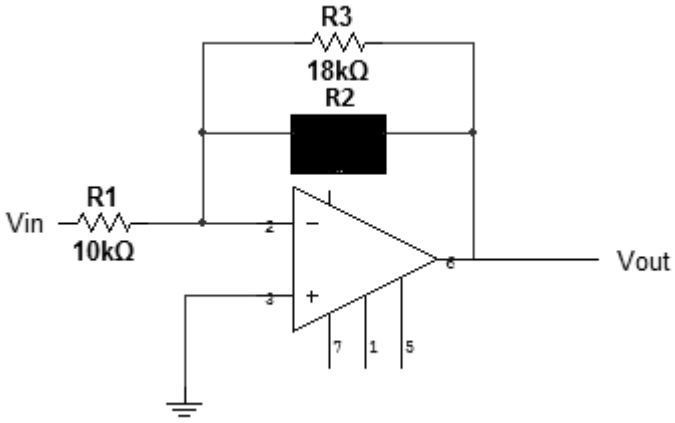


Figure 9: Circuit diagram of constant current source

3.5. Preparation of organogels

The preparation of the organogels was carried out by fluid filled fiber mechanism as per the previously reported literature [16]. Surfactant mixture of SM-PM (1:2 weight ratio) was used as the organogelator. The organogels were prepared by altering the compositions of SM-PM, SO and DW. The compositions of the selected organogels have been provided in table 1. Briefly, SM-PM mixture was dissolved in SO and subsequently homogenized using magnetic stirrer (100 rpm) at room-temperature (RT, 25 ^{o}C). To this homogenized solution, DW was added drop-wise with continuous vortexing. After the addition of DW, the mixture was vortexed further for 3 min. Drug (SA) containing organogels were prepared by using SA solution in DW as the aqueous phase. The final concentration of the drug was maintained as 0.5% w/w in all the gels.

Table 1: Composition of the organogels

Samples	Composition % (w/w)			SA % (w/w)
	SM	DW	SO	
F1	50.0	20.0	30.0	--
F2	60.0	20.0	20.0	--
F3	50.0	30.0	20.0	--
F1D	49.5	20.0	30.0	0.5
F2D	59.5	20.0	20.0	0.5
F3D	49.5	30.0	20.0	0.5

3.6. Impedance measurement

The electrical properties of the organogels were measured using a computer-controlled impedance analyzer (Phase sensitive multimeter, Model: PSM1735, Numetriq, Japan) in the frequency range of 0.1Hz–1.0 MHz

3.7. *In vitro* drug delivery

The drug delivery studies were performed using a specially designed diffusion cell (figure 5). SS electrodes (diameter: 2 cm) were used as the electrode and were connected to the donor and the dummy chambers. The donor chamber contained drug loaded organogel while the dummy chamber contained normal saline (figure 5). The donor and the receptor chambers were separated from the receptor chamber using a pre-activated dialysis membrane. The experimental set up of the iontophoretic drug delivery system has been shown in figure 10. The current flowing through the system was 1.06 mA, which provided a current density of 0.048 $\mu A/cm^2$. The effect of application of various waveforms on the release profile of the drug were used studied. The study was conducted for 4 h. 3 ml of the receptor volume was sampled at regular intervals of time (15 min during the first hour and 30 min thereafter). 3 ml of the receptor volume was replaced with fresh DW. The samples were then analyzed spectrophotometrically using a UV-visible spectrophotometer (UV-3200, LabIndia, Mumbai, India) at a λ_{max} of 294 nm.

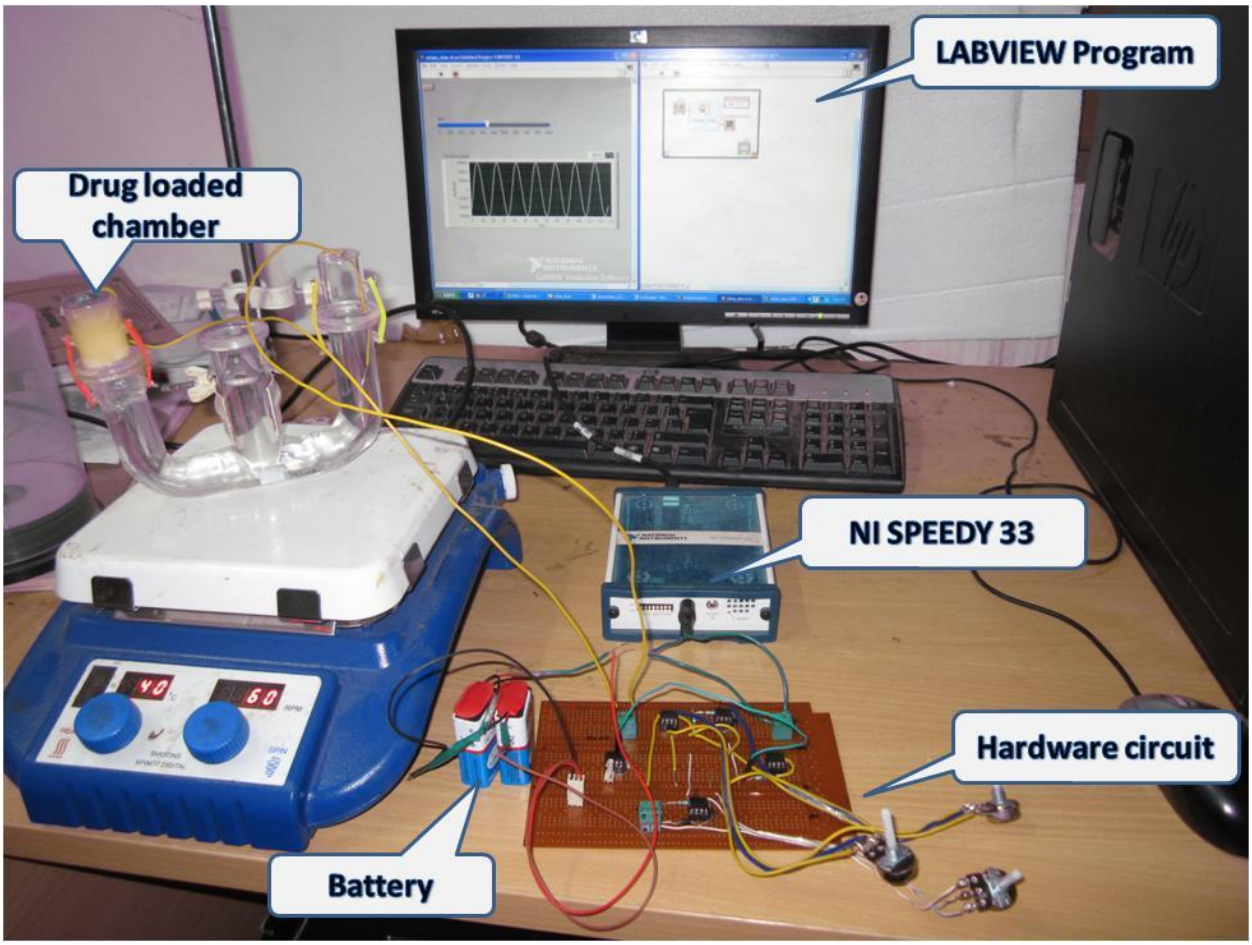


Figure 10: Experimental setup of iontophoretic drug delivery system

Chapter 4

Results and discussion

4.1. Waveform generator circuit development

The basic waveforms (Amplitude: 3.00 Vpp; Frequency: 440 Hz) were generated using computer controlled SPEEDY-33. The LABVIEW 8.6 was used for controlling the hardware. The LABVIEW program used for the generation of the basic waveforms (e.g. sine, square and triangular) has been shown in figure 9. The generated basic wave forms on front panel of the LABVIEW have been given in figure 10. The duty cycle of the square wave was 50%. The output of the SPEEDY-33 was fed into the voltage buffer. The output of the voltage buffer was same as that of its input due to the unity gain of the circuit [17]. The voltage buffer was used to provide protection to the SPEEDY-33. The output of voltage buffer (figure 11) was fed into the SCCs which modulated the basic signals being generated. The modulated signals have been shown in figure 12. The modulated signals (table 3) served as the input for the CCS.The modulated signals were generated with the help of SSC. The sine waveform was passed through the half wave rectifier circuit and the modulated signal was generated as a half wave rectified of sinusoidal waveform. While sine waveform was passed through the full wave rectifier circuit then modulated signal was generated as full wave rectified signal of the sinusoidal waveform. The square waveform was passed through the half wave rectifier circuit then the modulated signal was generated as pulse DC of square waveform.

Table 2: Basic waveforms

Basic waveform	Amplitude of basic waveform (V_{pp})	Frequency of basic waveform (Hz)	Signal conditioning circuit	Modulated waveform
Sinusoidal	3.00	440	--	SN
Square	3.00	440	--	SQ
Triangular	3.00	440	--	TR
Sinusoidal	3.00	440	Half-wave rectifier	SNH
Square	3.00	440	Half-wave rectifier	SQH (pulsed DC)
Sinusoidal	3.00	440	Full-wave rectifier	SNF

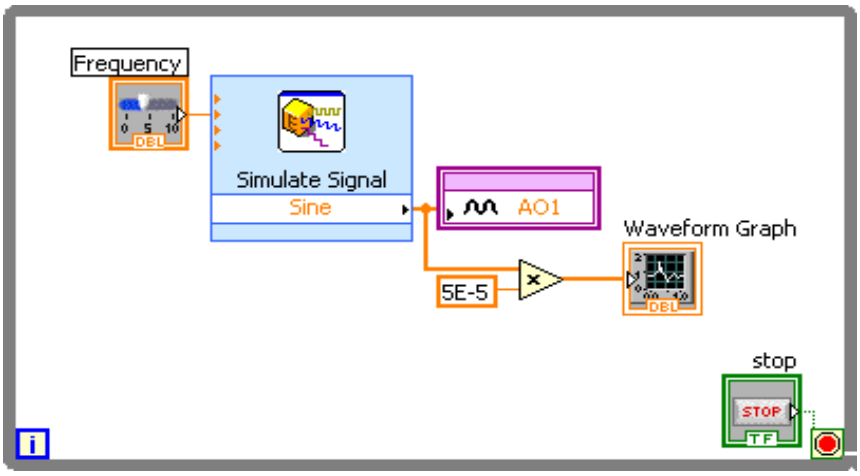
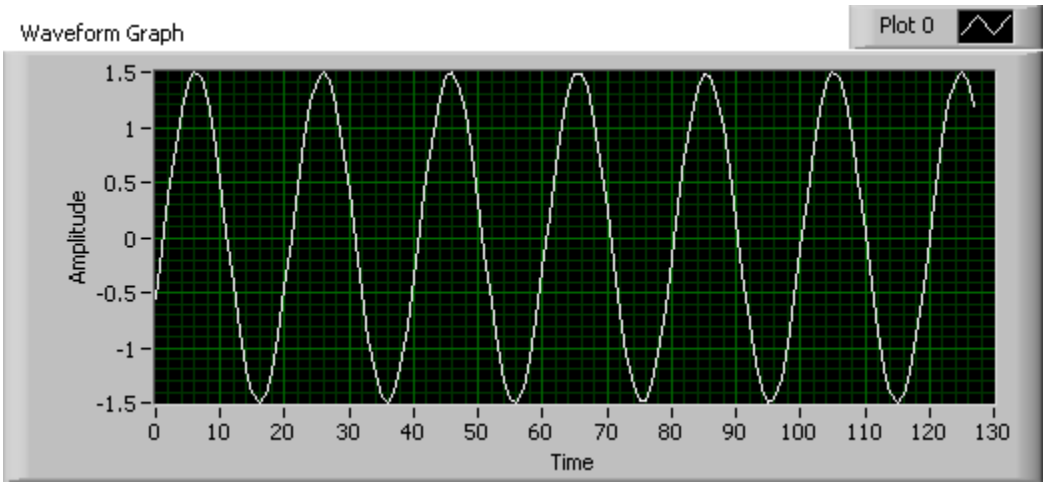
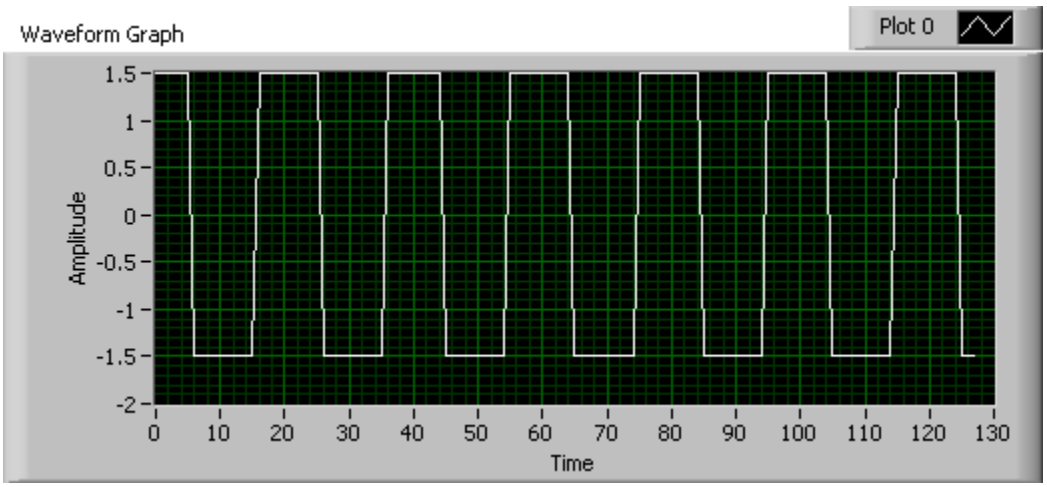


Figure 11: The LABVIEW programme for generation of basic wave forms





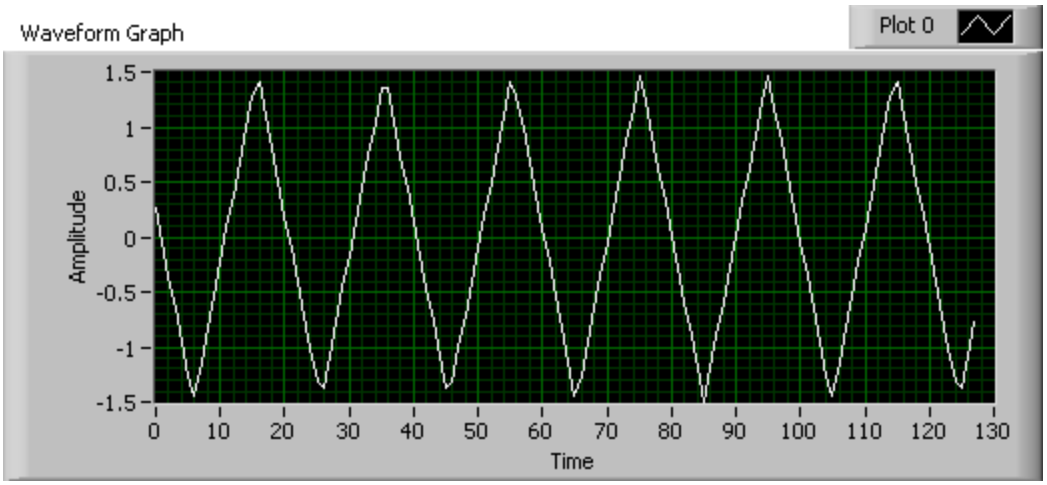
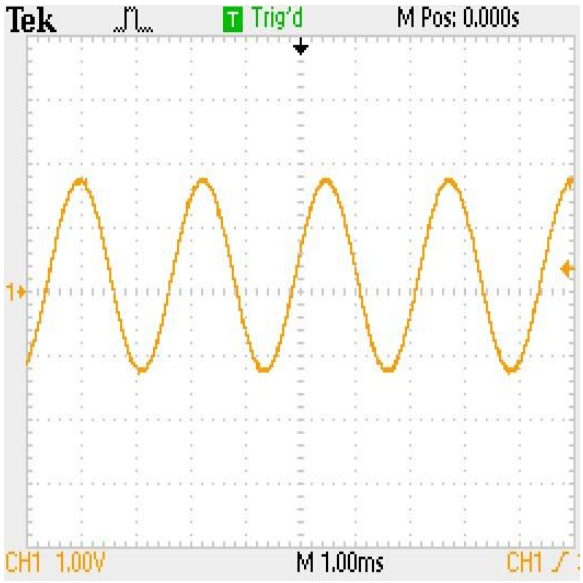
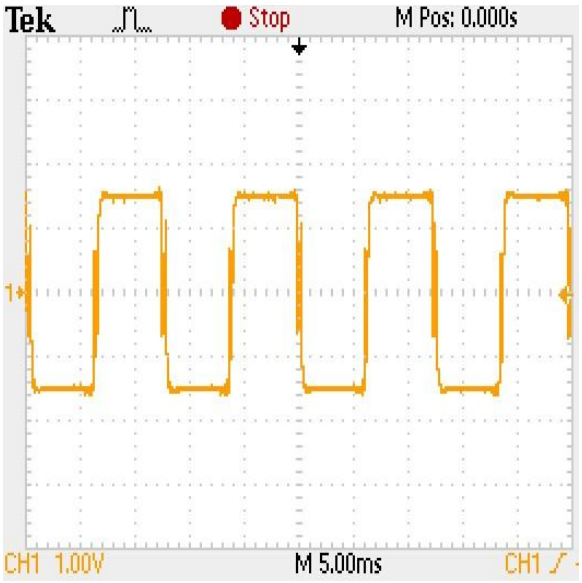


Figure 12: LabVIEW programme generated basic waveforms: (a) SN, (b) SQ, and (c) TR





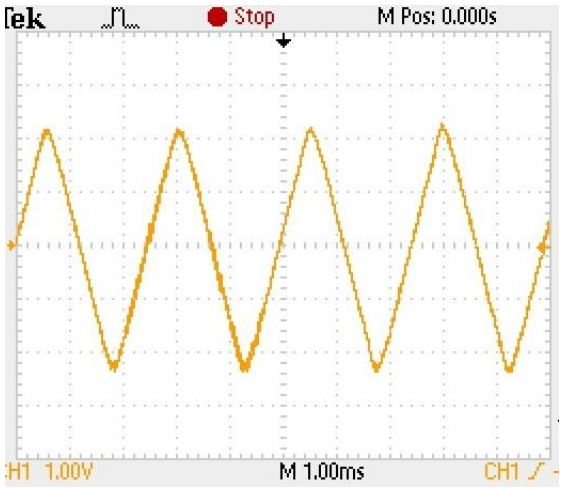
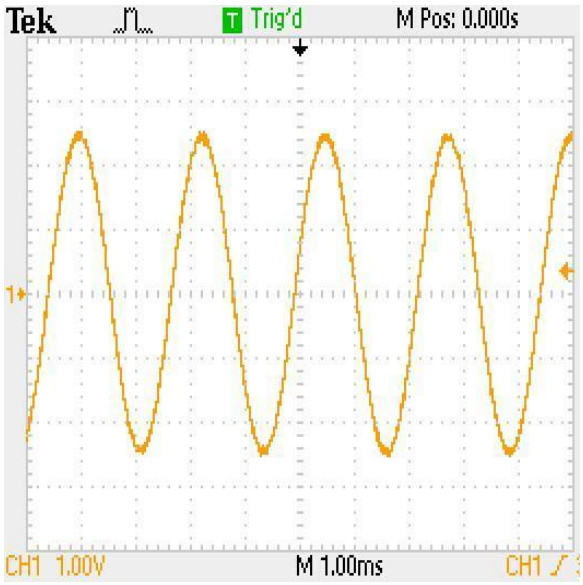
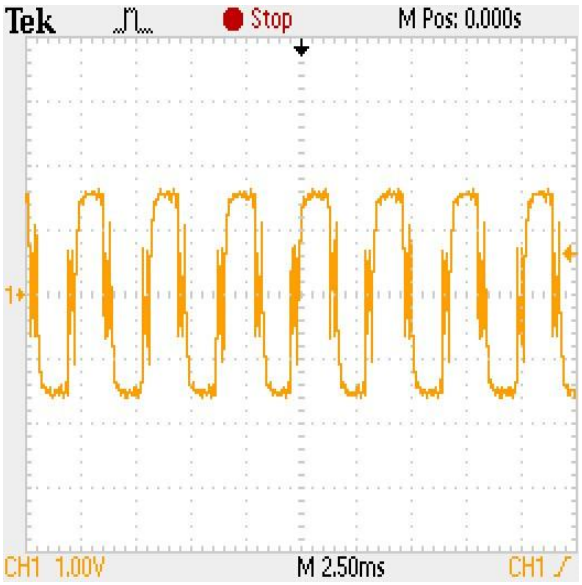


Figure 13: Output waveforms of the voltage buffer: a) SN, (b) SQ, and (c) TR





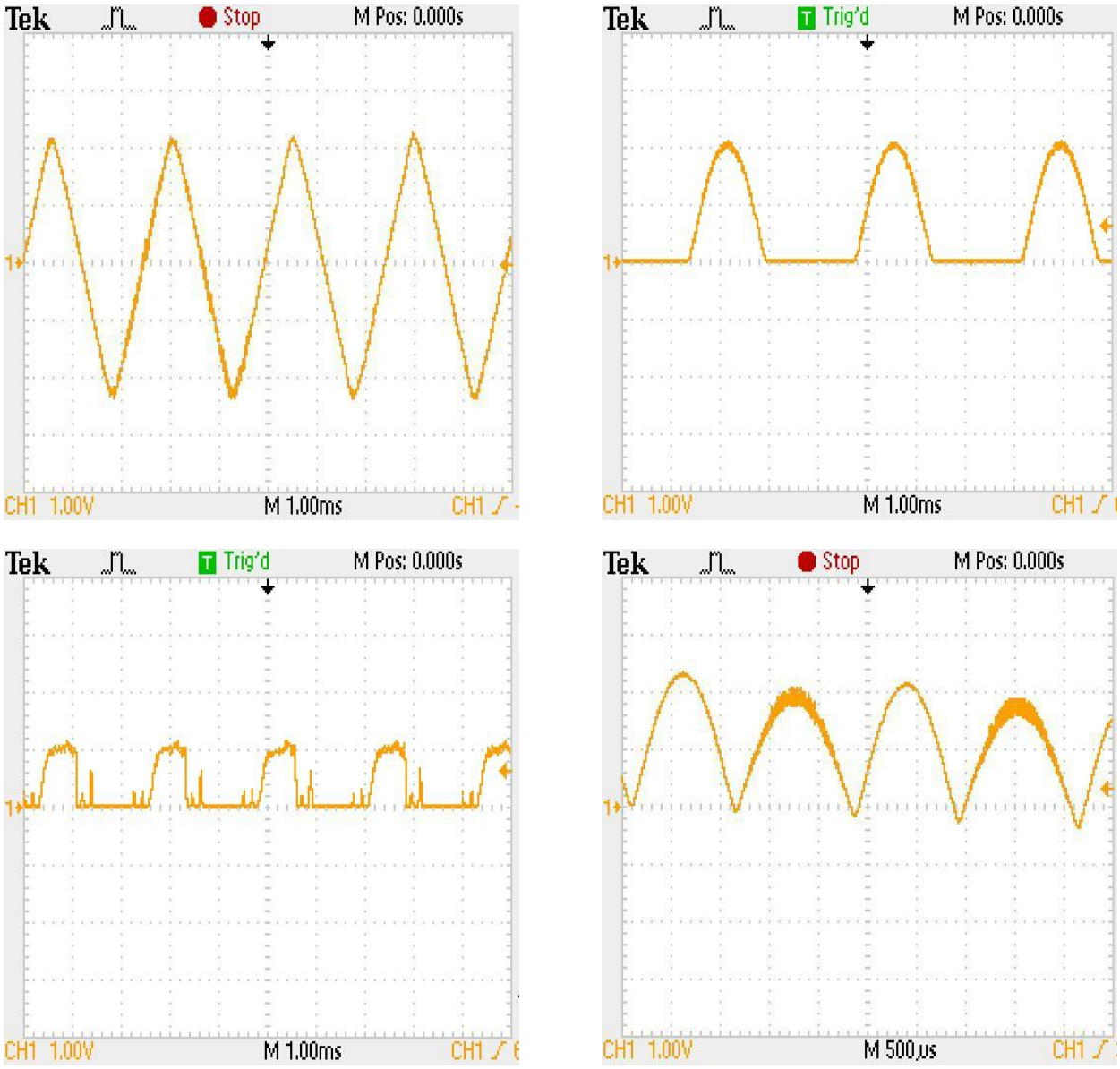


Figure 14: Output waveform of the signal conditioning circuit: (a) SN, (b) SQ, and (c) TR (d) SNH (e) SQH and (f) SNF

4.2. Stability of constant current source

The stability of constant current source was checked by the varying the load resistance of constant current source and measured the output voltage across it. The output voltage was measured at every stage by changing the load resistance. The output voltage has been shown in the table 4.The constant current source was saturated when the load resistance was more than 6.0 MΩ. The graph was plotted between the output peak to peak voltage (Pk-Pk) and load resistance (MΩ). The graph has been shown in figure 13.

Table 3: stability of constant current source

Load resistance (MΩ)	Output voltage (Pk-Pk)
1	5.12
2	5.16
3	5.2
4	5.25
5	5.26
6	5.28

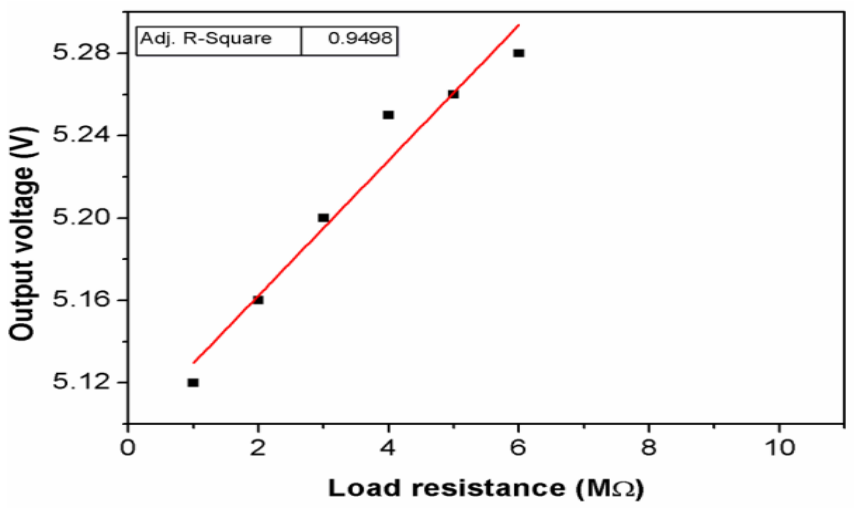


Figure 15: Stability of the CCS

4.3. Preparation of organogels

The solution of SM-PM mixture in SO was light brown in color. Addition of DW resulted in the formation of yellowish white or milky white colored semi-solid formulations (figure 14). The formation of organogels was confirmed by inverted test-tube method [18]. The formulations were regarded as organogels if they did not flow under gravity (figure15) (table 5). Stable gels were formed after the incorporation of 0.5% (w/w) SA into the organogels.

Table 4: The stable organogels, tested by inverted tube method

Samples	W/S atio	Result
F1	0.4	Gel formed
F2	0.3	Gel formed
F3	0.6	Gel formed
F1D	0.404	Gel formed
F2D	0.336	Gel formed
F3D	0.606	Gel formed

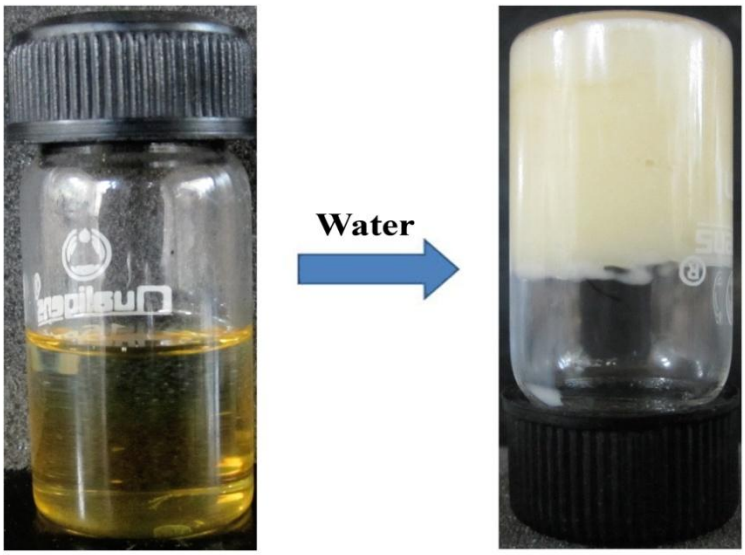


Figure 16: Formation of organgels

Figure 17: The stable organogels: (a) F1, (b) F2 and (c) F3

4.4. Impedance analysis

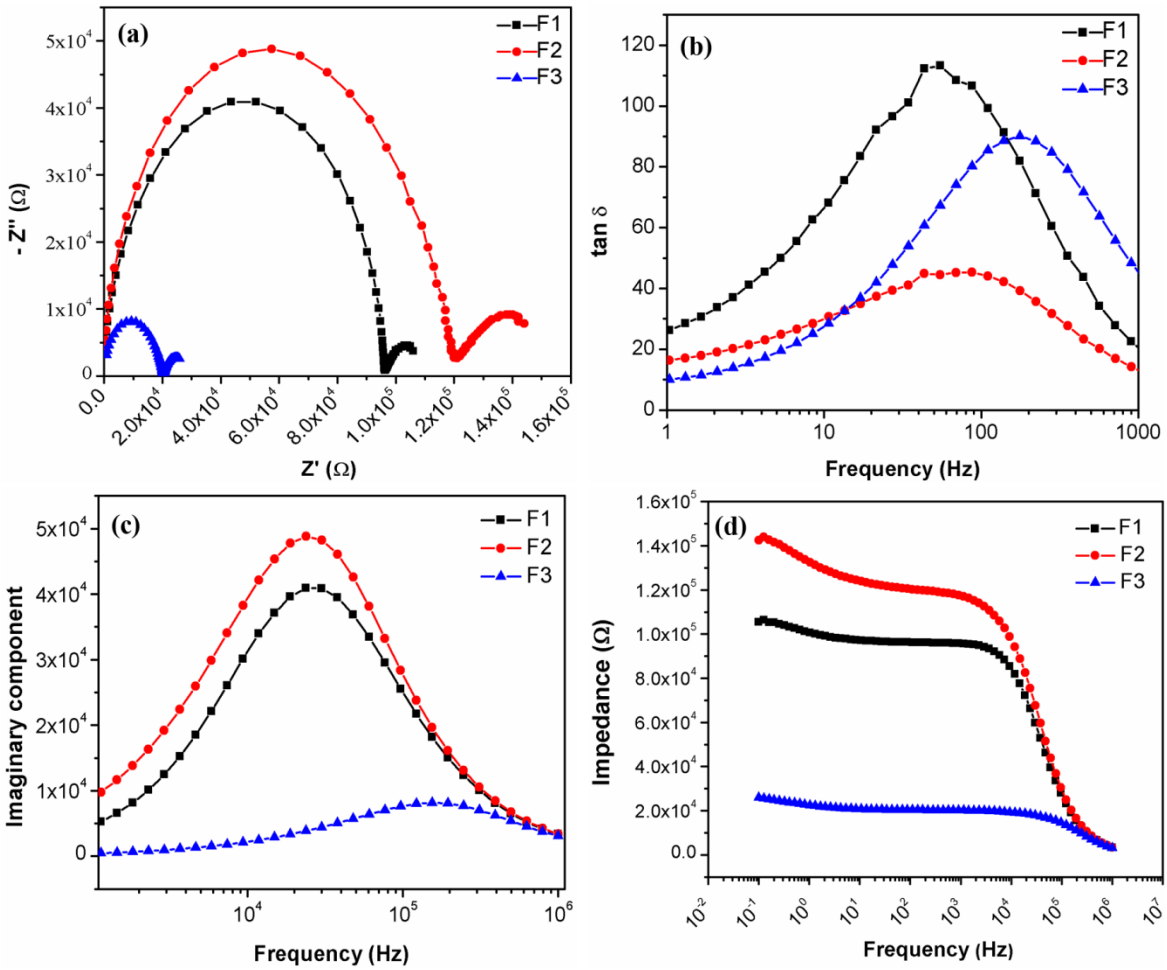


Figure 18: Electrical properties of F1, F2 and F3 gels (a) Nyquist plot (b) frequency vs tan δ (c) frequency vs impedance and (d) frequency vs imaginary component

The Nyquist plots of F1, F2 and F3 at RT have been shown in figure 20a. The intercept of the semicircle on the real axis gives bulk resistance of the materials. There was a decrease in the bulk resistance (R_b) of the organogels in the following order F2> F1>>F3. The least resistance of the F3 organogels may be attributed to the presence of higher proportion of water. Similarly, the higher resistances of F1 and F2 may be explained due to the presence of lower proportion of DW in these organogels.

The frequency dependant tan δ plot has been shown in figure 20b. The organogels have shown a single relaxation peak. This may be was due to the ionic transport process in the bulk.[19] The impedance vs. frequency plot has been shown in figure 20c. It was seen that F2 had the highest

impedance as compared to F1 and F3 and was in accordance with the bulk resistances of the organogels obtained from the Nyquist plot. The results showed that there was a decrease in the impedance of the organogels with the increase in the frequency. The variation of frequency vs. imaginary component of the organogels has been shown in Figure 20d. The relaxation time of the organogels (table 8) was calculated from the following equation (2):

$$2\pi f_{max}\tau_m = 1 \qquad (2)$$

where,

f_{max}= frequency at Z" max.

τ_m = Relaxation time

It was observed that the relaxation time (τ_m) of F3 was maximum as compared to F1 and F2. This might be associated with the presence of high water content F3. This resulted which led to the increased mobility of the charged particles within the gel systems [20].

Table 5: Bulk resistance and relaxation time of the organogels

Samples	**Bulk resistance (R_b) (Ω)**	**Relaxation time (Hz^{-1})**
F1	96241.6704	3907.93
F2	119697.912	3848.426
F3	19831.1861	29891.94

***4.5 In vitro* drug release studies:**

The *in vitro* drug release profiles from the organogels under different patterns of injected current have been in figure 26. The height and diameter of the donor chamber was 3.62 cm and 2.5 cm, respectively. 15 g of organogel was used for the study. The drug release studies suggested that the cumulative percent drug release (CPDR) from the organogels were higher when electrical current was applied as compared to the passive diffusion. The effect of the applied waveform shapes on the release of the drug has been tabulated in table 14. Under the experimental conditions, the triangular waveform and the pulsed DC have enhanced the drug release to the greatest extent (table 15). .In general, the effect of current on the release of the drug was more in

F1D and F2D as compared to F3D organogels. This may be due to the higher firmness of F3D which might have restricted the movement of drug molecules.

The drug release kinetics was predicted by best-fit model estimation. Data fitting was performed upon the 60 % of the total drug released. The results suggested that the release of the drug was found to follow Zero order kinetics under both passive and active conditions (figure 27 and table 16). This suggested that the release of the drugs was predominantly by diffusion and the release was concentration independent under the experimental conditions [21-22]. The results indicated that the application of current of different waveform did not alter the mechanism of drug release but only facilitated the active diffusion of the drug.

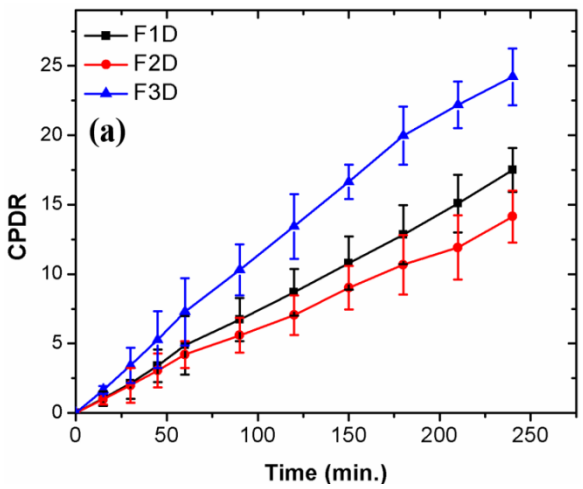
The Krossmeyer-Peppas (KP) release exponent (n) value was calculated from the slope of the KP model (figure 28). The n was found to be ≥1 in most of the cases (table 16). The results indicated that Case-II or super Case-II transport phenomena by the drug molecules. This kind of phenomena happen when the diffusion of the drugs are much faster as compared to the relaxation of the polymer molecules of the delivery matrices [23]. In some cases, the n value was found to be greater than 0.85. This suggested that the release of the drugs from these matrices followed anomalous release behavior. The increase in the CPDR values when an electric current was applied was more prominent in F1D followed by F2D and F3D.

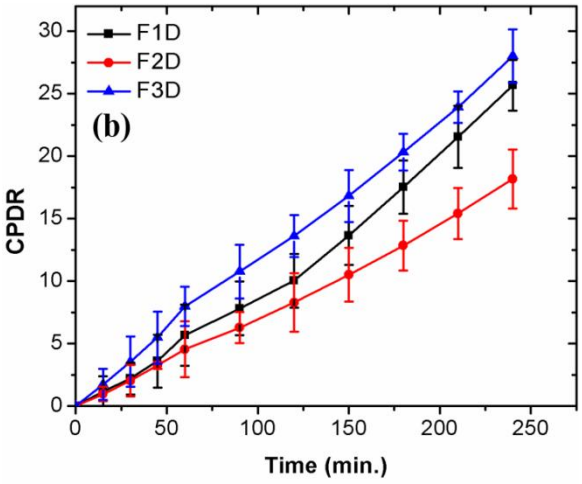
Table 6: The CPDR values of organogels

Type of wave form	**CPDR values**		
	F1D	**F2D**	**F3D**
Passive diffusion	17.5	14.16	24.2
SN	25.67	18.18	28.01
SQ	30.40	16.87	31.64
TR	27.13	29.80	32.18
SNH	21.16	32.36	32.16
SQH	24.87	26.82	34.95
SNF	24.44	22.37	39.65

Table 7: The % increase in CPDR due to iontophoresis over passive drug delivery

Type of wave form	F1D	F2D	F3D
SN	46.68	28.39	15.74
SQ	73.71	19.13	30.74
TR	55.02	110.45	32.97
SNH	20.91	128.53	32.89
SQH	42.11	89.40	44.42
SNF	39.65	57.98	63.84





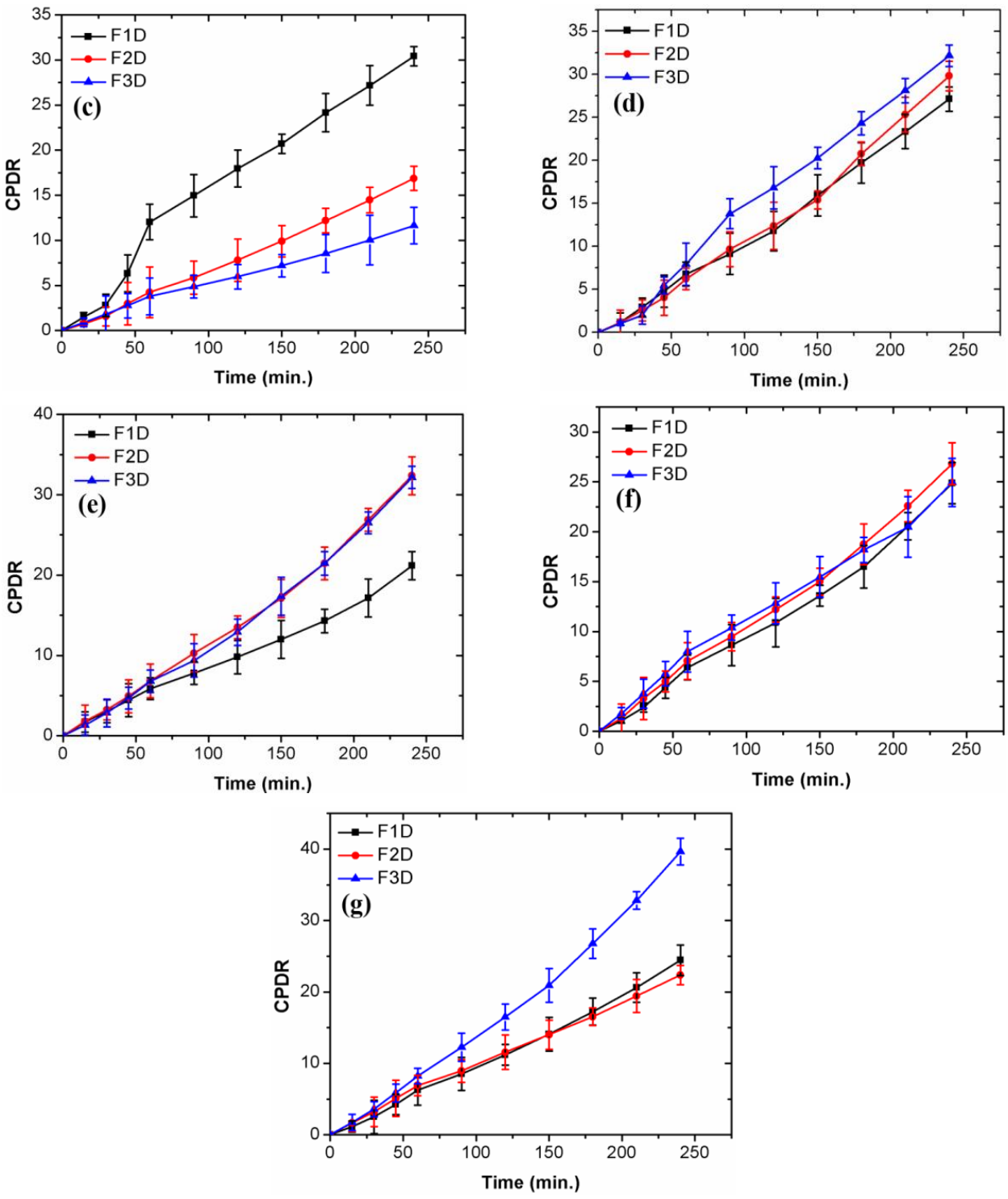
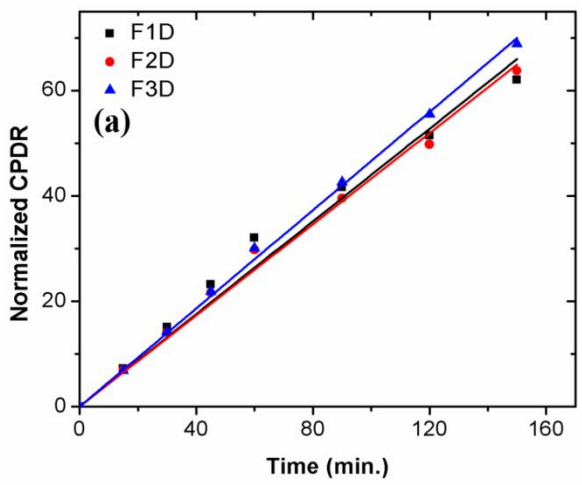
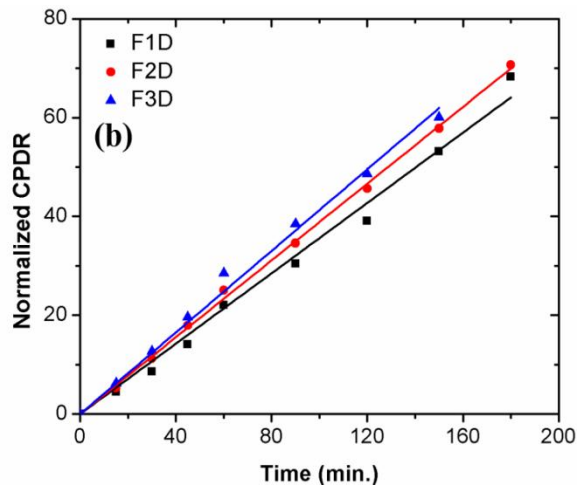
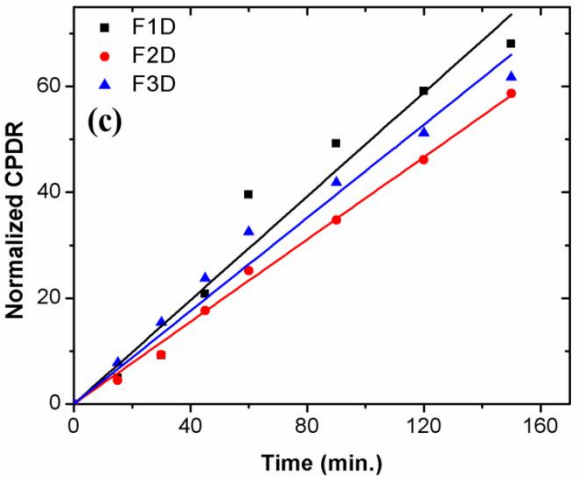
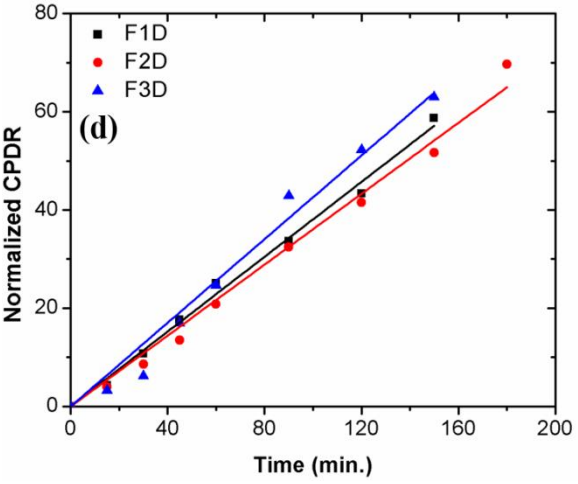


Figure 19: The *in vitro* drug delivery profiles under (a) passive diffusion and (b) SN, (c) SQ (d) TR (e) SNH (f) SQH and (g) SNF wave forms.


F1D
F2D
F3D
(a)
Normalized CPDR
Time (min.)
0
20
40
60
0
40
80
120
160


F1D
F2D
F3D
(b)
Normalized CPDR
Time (min.)
0
20
40
60
80
0
40
80
120
160
200


F1D
F2D
F3D
(c)
Normalized CPDR
Time (min.)
0
20
40
60
0
40
80
120
160


F1D
F2D
F3D
(d)
Normalized CPDR
Time (min.)
0
20
40
60
80
0
40
80
120
160
200

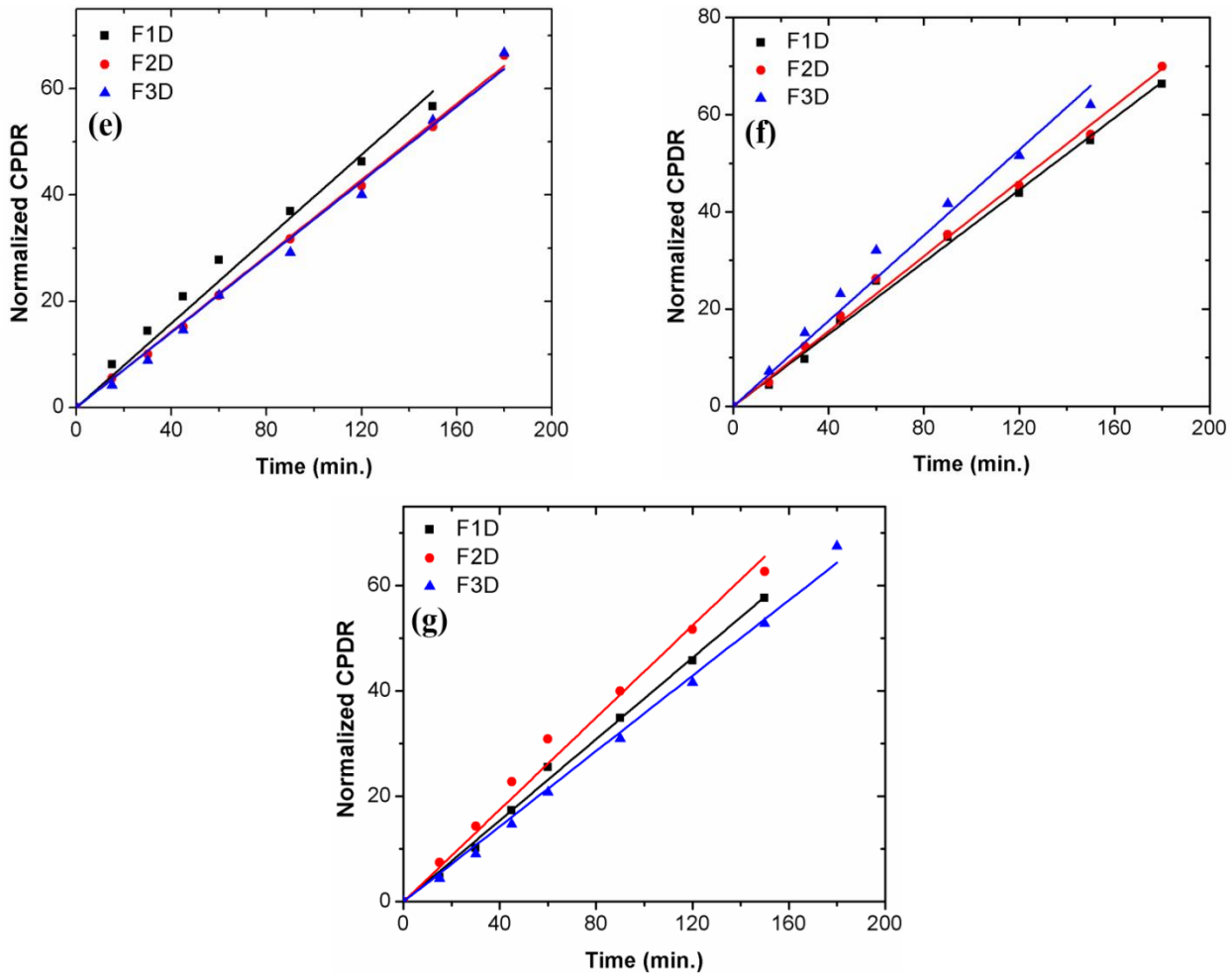
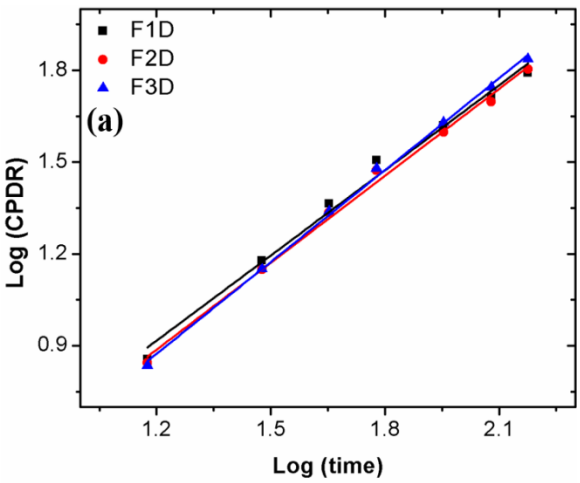
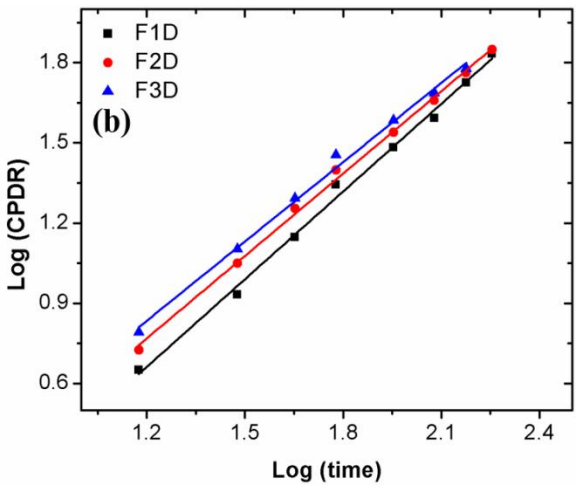
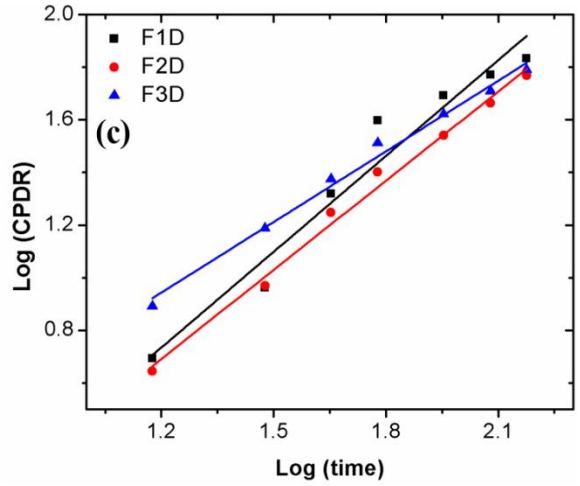
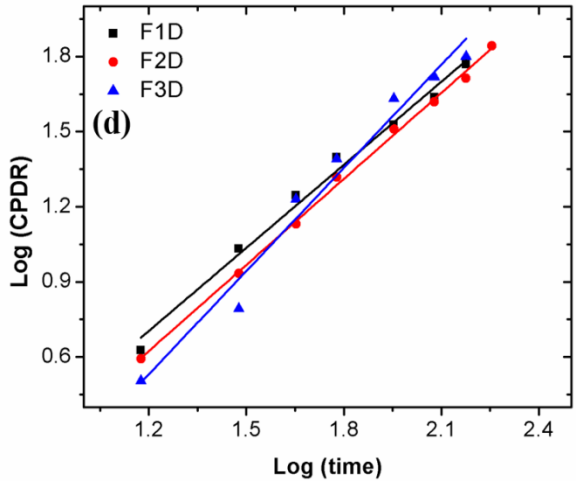


Figure 20: The zero order kinetics of *in vitro* drug delivery under (a) passive diffusion and (b) SN, (c) SQ, and (d) TR (e) SNH (f) SQH and (g) SNF wave forms.


F1D
F2D
F3D
(a)
Log (CPDR)
Log (time)
1.8
1.5
1.2
0.9
1.2
1.5
1.8
2.1


F1D
F2D
F3D
(b)
Log (CPDR)
Log (time)
1.8
1.5
1.2
0.9
0.6
1.2
1.5
1.8
2.1
2.4


F1D
F2D
F3D
(c)
Log (CPDR)
Log (time)
2.0
1.6
1.2
0.8
1.2
1.5
1.8
2.1


F1D
F2D
F3D
(d)
Log (CPDR)
Log (time)
1.8
1.5
1.2
0.9
0.6
1.2
1.5
1.8
2.1
2.4

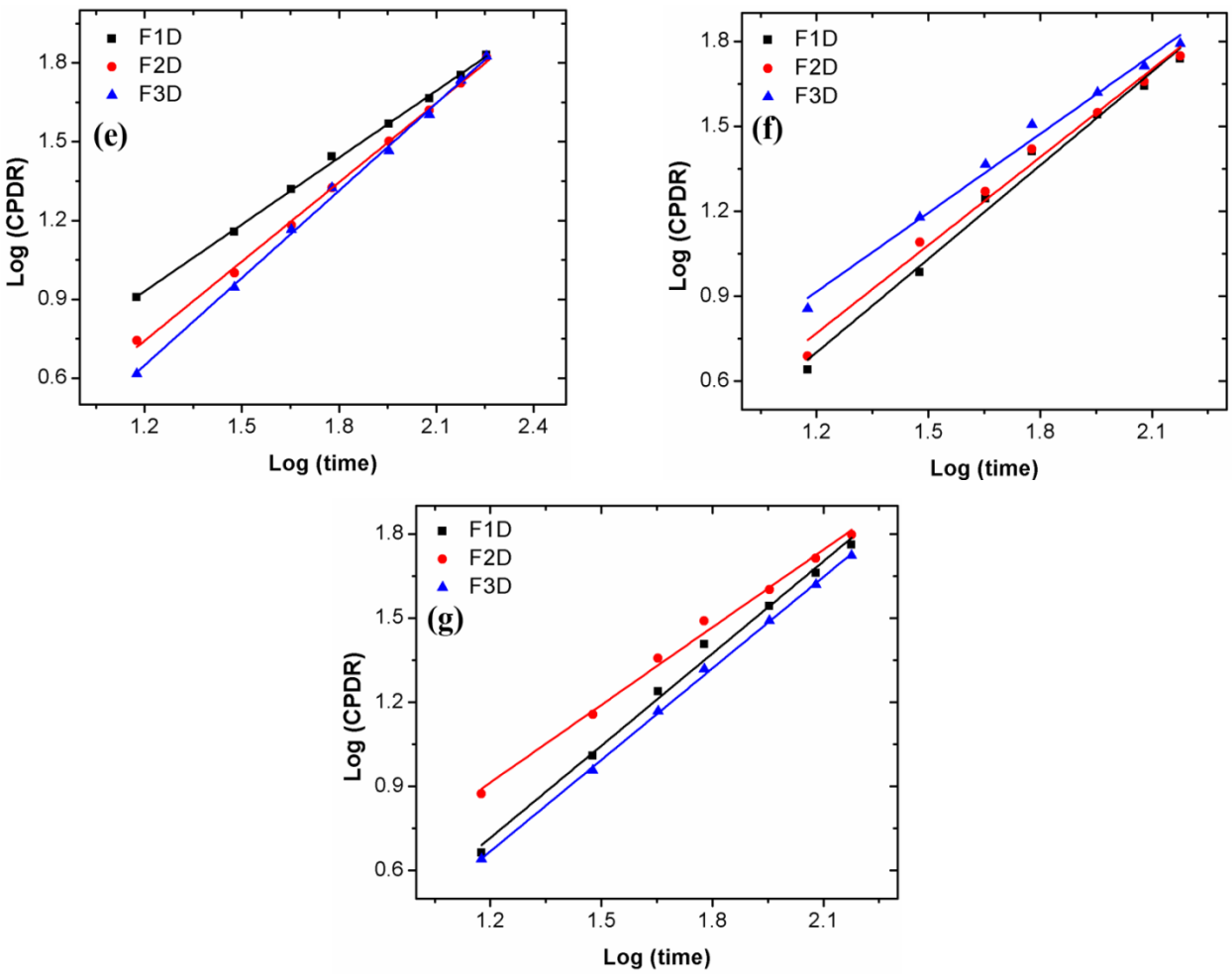


Figure 21: The KP kinetics of *in vitro* drug delivery under (a) passive diffusion and (b) SN, (c) SQ, and (d) TR (e) SNH (f) SQH and (g) SNF wave forms.

Table 8: The drug release kinetics

Wave form	Sample code	Zero order (r^2)	Higuchi (r^2)	KP (r^2)	n	Best fit model
Pas	F1D	0.9791	0.9791	0.99	0.9284	Zero order
	F2D	0.9921	0.8687	0.99	0.9475	Zero order
	F3D	0.9982	0.8679	0.99	1.0014	Zero order
SN	F1D	0.99	0.8096	0.99	1.0931	Zero order
	F2D	0.9988	0.8585	0.99	1.0272	Zero order
	F3D	0.9931	0.8804	0.99	0.9883	Zero order
SQ	F1D	0.9989	0.8018	0.95	1.214	Zero order
	F2D	0.9962	0.8386	0.99	1.13	Zero order
	F3D	0.974	0.9173	0.99	0.8954	Zero order
TR	F1D	0.9944	0.8434	0.98	1.1054	Zero orde
	F2D	0.9956	0.8059	0.99	1.14	Zero order
	F3D	0.9795	0.7957	0.97	1.37	Zero order
SQH	F1D	0.9953	0.8617	0.99	1.0818	Zero order
	F2D	0.9961	0.8786	0.99	1.0272	Zero order
	F3D	0.9391	0.9096	0.97	0.9284	Zero order
SNH	F1D	0.9865	0.9085	0.99	0.8477	Zero order
	F2D	0.9982	0.8367	0.99	1.0053	Zero order
	F3D	0.9931	0.8126	0.99	1.10	Zero order
SNF	F1D	0.9968	0.8493	0.99	1.094	Zero order
	F2D	0.9871	0.8999	0.98	0.9228	Zero order
	F3D	0.9953	0.8312	0.99	1.0937	Zero order

Chapter 5

Conclusion

5. Conclusion

In the current study, a computer controlled iontophoretic drug delivery system was successfully developed. The system was tested by using span 80-Tween 80 based sunflower oil containing organogels. SA was used as the model drug during the study. The *in vitro* SA release was performed under different wave forms and compared against passively diffused drug across the in built iontophoretic set up. Potential enhancement of CPDR under the influence of current was seen against passively diffused drug. The results suggested that the developed iontophoretic set up has potential application in the iontophoretic drug delivery system.

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