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Preparation and Evaluation of Controlled Release of Eperisone Hydrochloride Resinate Beads by Complexing with Ion Exchange Resin

Vijay Sharma*, Pankaj Arora

Abstract

Complexes of ion-exchange resins and Eperisone hydrochloride, a model drug, were prepared using a batch method with different functional groups, loading equilibrium time, degree of cross linking, and resin particle size. Drug loading efficiency, mircromeritics properties and study of effect of cross linking and particle size on release behaviours, were also investigated. Most of the functional groups of resins were loaded with EpeH after the completion of a single batch method and it was recommended for drug loading into the ion-exchange resin. Using a batch method, drug loading could be monitored by simply measuring changes in the pH of the reaction medium since as complex formation reached completion, the pH returned to the initial pH of the eluent due to the limited amount of functional groups available for the exchange. EpeH could be loaded up to the ratio of 1 (drug): 1 (resin), depending on the physicochemical properties of the resin. As the cross linking ratio and particle size increased, release rate decreased due to the reduced effective diffusion coefficient and surface area.

Keywords: Amberchrom, Eperisone HCl, Ion exchange resins

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Introduction

In last few years, ion exchange resins have been extensively studied and researched due to their verasatile properties as drug delivery vehicles in novel development of pharmaceuticals.[1] Ion exchange resins contain ionizable groups distributed regularly along the polymer backbone. IER simply insoluble polyelectrolyte's.[2,3] Ion exchange resin mostly used for taste masking of drug and for controlling the release of drug by preparation of drug resin complex in which drug is loaded.[4,5]

Eperisone hydrochloride, which is chemically known as 4-ethyl-2-methyl-3-piperidino propiophenone hydrochloride, is an antispasmodic drug. Eperisone HCl basically work on both skeletal muscles and vascular muscle by relaxing them.[6] Eperisone HCl reduce myotonia, improve the blood flow, and suppression of the pain reflex.[7,8] The half-life of Eperisone hydrochloride is from 1 to 1.8 h. Eperisone HCl can be formulated as controlled release dosage form because it has a short half-life and dosing frequency is 3 times a day.[8]

Materials and Methods

Eperisone hydrochloride, a model drug, was obtained from the SNA laboratories Ltd. Mumbai Ion-exchange resins (Amberchrom 50wx4 50–100, Amberchrom 50wx4 100–200, Amberchrom 50wx4 200–400, Amberchrom 50wx8 100–200 Amberchrom 50wx8 200–400) were provided by Alkind phama.

Analysis of Eperisone Hydrochloride

Determination of melting point

Melting point was determined by small amount of Eperisone hydrochloride in capillary tube closed at one end. In electrically operated digital melting point apparatus, the capillary tube was placed and the temperature (which the drug melts) was recorded. This was performed 3 times and average value was note down.

Department of Pharmacy, Faculty of Pharmacy, Lords University, Alwar, Rajasthan, India

Corresponding Author: Vijay Sharma, Department of Pharmacy, Faculty of Pharmacy, Lords University, Alwar, Rajasthan, India. E-mail: vijas007@gmail.com

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FT-IR spectroscopy

The FT-IR analysis of the sample was carried out for qualitative compound identification and compatibility between Eperisone hydrochloride and the selected resins. The pure drug and drug with resins were scanned separately. Potassium bromide was mixed with drug and/or resins in 9:1 ratio and the spectra were taken over a wavelength of 4000 $cm^{-1}$to 400 cm^{-1}. FT-IR spectrum of Eperisone hydrochloride was compared with FT-IR spectra with resins.

Solubility

The solubility of Eperisone hydrochloride was determined in different solvents such as distilled water.0.1 N HCl, ethanol, and various pH solutions. An excess quantity of the drug was added in 10 ml of each solvent in screw capped glass test tubes and shaken or 12 h at room temperature. The solution was filtered, diluted, and the solubility was determined spectrophotometrically.

Partition coefficient

The partition coefficient study was performed using n-octanol as oil phase and distilled water as aqueous phase. The two phases

were mixed in an equal quantity and were saturated with each other on a mechanical water bath shaker at 32°C for 24 h. The saturated phase was separated. Each volume (10 ml each) of two phases was taken in a separating funnel and, this mixture 100 mg of weighed amount of drug was added. The separating tube was shaken for 24 h to complete partitioning. The two phases were separated by separating funnel. And they were analyzed for respective drug contents. The partition coefficient of drug $K_{o/w}$ was calculated using following formula.

$$Ko/w = \frac{Concentration\ in\ octanol}{Concentration\ in\ distilled\ water}$$

Calibration curve of Eperisone hydrochloride

Accurately weighed quantity of Eperisone hydrochloride was dissolved in distilled water and made up to 100 ml with distilled water. Appropriate aliquots were taken into different volumetric flasks and volume was made up to 10 ml with distilled water so as to get drug concentration of 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 μg/ml. The absorbencies of these drug solutions were estimated at λ_{max} 261 nm. The data are obtained and constructed a calibration curve.

Purification of ion exchange resins

Cationic ion exchange resins were purified using the method reported by Irwin *et al*. According to the method reported that the resin (30 g) was washed successively with distilled water(300 ml), methanol (300 ml), benzene (300 ml), followed by washing with distilled water several times to eliminate organic and colour impurities. The wet resins were dried over night in hot air oven at 50°C and kept in amber glass vials.

Preliminary Evaluation of Resins

Evaluation of physical properties

The size of cationic ion exchange resins was determined by microscopic method. Size analysis was carried out using optical microscopic method. The size distribution data were obtained using calibrated eyepiece micrometer and the average diameter was calculated. The IER were dispersed in liquid paraffin and observed under microscopic magnification 10-×10X. The diameters of 300 particles were determined randomly using 14.28 as calibration factor. Water absorption was obtained by keeping 500 mg of resin in contact with 1 ml of water in a petridish. The time required for complete water absorption was recorded.

Micromeritics properties of Ion exchange resins

The flow of ion exchange resins was found to be good flow.

Bulk density

Bulk density of IER was determined by pouring gently 20 gm of sample through a glass funnel into 50 ml graduated cylinder. The volumes occupied by the samples were recorded. Bulk density was calculated as:

$$Bulk\ density = \frac{Weight\ of\ sample\ in\ gm}{Volume\ occupied\ by\ the\ sample}$$

Tapped density

Tapped density was determined using electrolab density tester, which consists of a graduated cylinder mounted on a mechanical tapping device. An accurately weighed sample of powder was carefully added to the cylinder with the aid of a funnel. Typically, the initial volume was noted, and the sample is then tapped (100 tapping) until no further reduction in volume is noted or the percentage of difference is not more than 2%.

A sufficient number of taps should be employed to assure reproducibility for the material in question. Volume was noted and taped density is calculated using following formula.

$$Tapped\ density = \frac{Wt.\ of\ sample\ in\ gm}{Tapped\ volume}$$

Compressibility index and Hausner ratio

In recent years, the compressibility index and the closely related Hausner ratio have become the simple, fast, and popular methods of predicting powder flow characteristics [Table 1].

Both the compressibility index and the Hausner ratio were determined using bulk density and the tapped density of a powder.

$$Carr's\ index = \frac{Tapped\ desnity - Bulk\ density}{Tapped\ density} \times 100$$

$$Hausner's\ Ratio = \frac{Tapped\ Density}{Bulk\ Density}$$

Angle of repose

The angle of repose has been used to characterize the flow properties of solids [Table 2]. Angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles. This is the maximum angle possible between surface of pile of powder or granules and the horizontal plane.

$\tan\theta = (h/r)$

$\theta = \tan^{-1}(h/r)$

Where, θ = angle of repose, h = height, r = radius.

A funnel was fixed at a height approximately of 2–4 cm over the platform. The loose powder was slowly passed along the wall of funnel, till the cone of the powder formed. Determine the angle of repose by measuring the height of the cone of powder and radius of the heap of powder.

Effect of resin activation

To study the effect of method of resin activation on the complexation of drug with using the resins were activated by different methods. Resin 200 mg placed on a whatmann filter paper in a funnel, washed with deionized water and subsequently with 1N HCl 100 ml. The resin was rewashed with water until neutral pH was reached. Similarly, alkali activation of resin was performed by placing the resin in 1N NaOH solution. Finally resins were also activated with combined treatment of 1N HCl and 1N NaOH solutions.

Preparation of Eperisone HCl-loaded resinate beads

The Eperisone resin complexes were prepared by a batch Process. The previously purified resin particles (1 g dry weight,) were

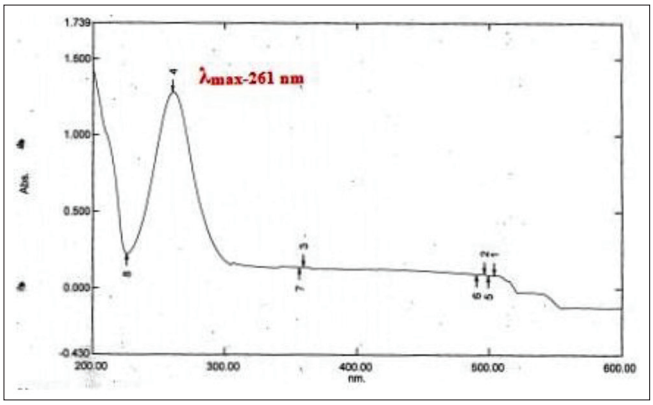

Figure 1: UV Spectrum of Eperisone hydrochloride in distilled water

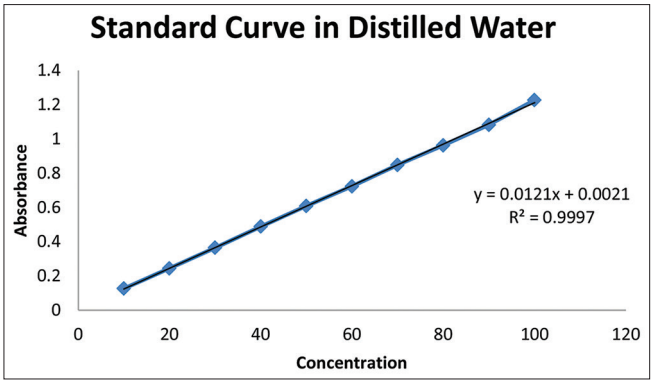

Figure 2: Calibration curve of Eperisone hydrochloride in distilled water

Table 1: Flow properties and corresponding angles of repose

Flow property	*Angle of repose (°)*
Excellent	25–30
Good	31–35
Fair - Aid not needed	36–40
Passable - May hang up	41–45
Poor - Must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

Table 2 : Relation of flow property with Hausner ratio and compressibility index

Compressibility index (%)	*Flow character*	*Hauser's ratio*
≤10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>38	Very, very poor	>1.60

dispersed in a 1.0 % (w/v) drug solution (100 ml) under magnetic stirring at room temperature for 5 h (single batch). To investigate how quickly equilibrium could be reached, 0.1 ml of supernatant was collected at predetermined intervals during complex formation at room temperature, diluted with water, and then the drug amount was quantified by spectrophotometrically at λ_{max} 261 nm. The complex was separated from the supernatant by filtration, washed with water to remove any uncomplexed drugs, and then dried in an oven at 40°C for 24 h.[9,10]

Evaluation of Drug Resin Complex

Differential scanning calorimetry (DSC) of Eperisone HCl resinate beads

DSC was used to determine the melting point and to determine the molecular properties of Drug resin complex of the sample. The DSC analysis was carried out with Shimadzu DSC 60 thermal analyser at the heating flow rate of 5°C/min between the ranges 50°C and 300°C under static air using aluminum pans.

FT-IR of Eperisone HCl resinate beads

The FT-IR analysis of the Dug resin complex sample was carried out for qualitative compound identification and compatibility between Eperisone hydrochloride and the selected resins (Amberchrom 50wx4 50–100, Amberchrom 50wx8 100–200. The pure drug and drug with resins were scanned separately. Potassium bromide was mixed with drug and/or resins in 9:1 ratio and the spectra were taken over a wavelength of 4000–400 cm^{-1}. FT-IR spectrum of Eperisone hydrochloride was compared with FT-IR spectra with resins.

Study of the effect of resin properties on in vitro release of Eperisone HCl from drug resinate beads

Drug release from different drug–resinate beads (Amberchrom 50wx4 50-100, Amberchrom 50wx4 100–200, Amberchrom 50wx4 200–400 Amberchrom 50wx8 100–200, Amberchrom 50wx8 200–400) was conducted according to USP 24 dissolution apparatus II (paddle method). The dissolution media were 900 ml distilled water and maintained at 37 ± 1° C. Rotation speed was 50 ± 1 rpm. An accurate weight of the drug resin complex, equivalent to 100 mg of Eperisone hydrochloride was added in dissolution medium while the solution was agitated using the paddle. A 1 ml of sample was collected and replaced with fresh medium at appropriate interval. An absorbance of sample was measured by UV spectrophotometer at 261 nm.[11,12]

Results

Analytical Profile of Drug

Determination of melting point

Melting point of Eperisone hydrochloride was performed 3 times and average value was found 183.0 ± 0.6. This result was in conformation to the standard text. The DSC studies also revealed that melting point at 183.5°C.

Determination of Absorption maxima (λ_{max}) in distilled water

The stock solution was prepared as per the method described in methodology section and scanned by UV-Visible spectrophotometer. The λ_{max} was found [Figure 1] to be 261 nm was taken as analytical wavelength. The UV absorption spectrum of Eperisone hydrochloride [Figure 1] showed peak at 261.0 nm against blank and the same was used for further analysis.

Calibration curve of Eperisone hydrochloride

The calibration curve was prepared and data obtained by the procedure described in methodology section where given in Table 3 and Figure 2. The data correlation coefficient of 0.999 and the equation of regressed line depicted as below

The linear regression analysis was done on absorption data point. The results are as follows

Parameters	*Eperisone Hydrochloride*
λ_{max} (nm)	261 nm
Beers Law Limits(µg/ml)	10–100 (µg/ml)
Regression equation	0.012x+0.002
Slope	0.012
Intercept	0.002
Correlation coefficient	0.999

Solubilty

The solubility of Eperisone hydrochloride was determined in different solvents. The solution was filtered, diluted, and the solubility was determined by spectrophotometrically and the observation is shown in Table 4.

Partition coefficient

The partition coefficient was determined by the shake flask method or tube method. The partition coefficient measuring the distribution of the solute is by UV spectroscopy [Table 5].

$$Ko / w = \frac{Concentration\ in\ oily\ phase}{Concentration\ in\ aqueous\ phase}$$

FT-IR studies

FT-IR studies were carried out for pure drug and along with ion exchange resins. They are summarized as follows. The FT-IR spectra of Eperisone Hydrochloride [Figure 3] exhibited peaks at 3054.76 cm^{-1} (C-H aromatic stretching), 2663.78 cm^{-1} (C-H aliphatic stretching), 3335.03 cm^{-1} (N-H amide bending), 1230.63 cm^{-1} (C-N bending), 1606.76cm^{-1} (C=C group), and 1120.68 (C-O group). Similarly, FT-IR spectra of Eperisone hydrochloride in combination with ion exchange resins and pure resins showed in Figures 3-7. The FT IR spectra of solid drug: Resin complex of Eperisone hydrochloride with different ion exchange resins indicated that the CH_2 group of drug interacts with SO_3H group of different resins. This is confirmed by spectral analysis. Drug and resin molecule shows overlap each over and significant reduction in the intensity of distinctive peaks of drug demonstrates the formation of complex. The peaks are given in the Table 6 can be considered as characteristic peaks of the Eperisone hydrochloride. This indicates that there is interaction between Eperisone hydrochloride and different resins and the drug was complexed with the resins.

The FTIR and solubility studies suggests that EpeH exists in the protonated drug ion which can displace the hydrogen counter - ion (H^+) at the sulfonic acid functional groups on the IER preparation.

$$Re–SO_3–H^+ + BH^+ \rightarrow Re–SO_3–BH^+ + H^+$$

DSC Study

DSC studies for pure drug, selected ion exchange resin and drug resinate beads were carried out. The thermogram of pure drug, ion exchange resin (Amberchrom 50 wx4 50–100) and drug resinate beads (Eperisone Hydrochloride + Amberchrom 50 wx4 50–100) is shown in the Figures 8-10, respectively. Thermogram of pure drug, presenting in Figure 8, indicates that melting of the drug is at 183.5°C. In the Figure 9 indicates that the melting of the ion exchange resin (Amberchrom 50 wx4 50–100) without drug has taken place at 104.6°C. The thermogram of DRC, presented in Figure 10 indicates that the melting of DRC (Eperisone Hydrochloride + Amberchrom 50 wx450–100) has taken place at 166.5°C. It could because the resins have undergone melt at 104.6°C. Before the resin completely melts, the drug might have started melting giving the broad peak that is 166.5°C.

Table 3: Calibration curve data for Eperisone hydrochloride in distilled water

S. No.	*Concentration (µg/ml)*	*Absorbance (261 nm)*
1.	10	0.126
2.	20	0.244
3.	30	0.364
4.	40	0.488
5.	50	0.608
6.	60	0.723
7.	70	0.848
8.	80	0.962
9.	90	1.082
10.	100	1.226

Table 4: Solubility of Eperisone hydrochloride in different solvents

S. No.	*Solvents*	*Solubility (mg/ml)*
1.	Water	64.76
2.	0.1 N HCl	64.58
3.	Methanol	68
4.	pH 2.2	66.14
5.	pH 6.8	64.14

HCl: Hydrochloride

Table 5: Partition coefficient of Eperisone hydrochloride

S. No.	*Aqueous phase*	*Oily phase*	*Eperisone HCl*
1.	Distilled Water	n-Octanol	1.35
2.	Buffer pH 1.2	n-Octanol	1.41
3.	Buffer pH 6.8	n-Octanol	1.42

HCl: Hydrochloride

Preliminary Evaluation of Resins

Evaluation of physical properties

The size of cationic ion exchange resins was determined by optical microscopic method. The average size of ion exchange resins particles was found within the range which is in confirmation with that reported in the literature. The water uptake time of resins were found to be 43–67 s. The result shows that ion exchange resins beings highly porous and even though insoluble in water are capable of hydration. The results were shown in Table 7. The water uptake time of selected IER was found to be directly proportionally to the particle size of the resins.

Micromeritics properties of ion exchange resin

The micromeritics properties of ion exchange resin such as angle of repose, bulk and tapped density, Carr's index, and Hausner's

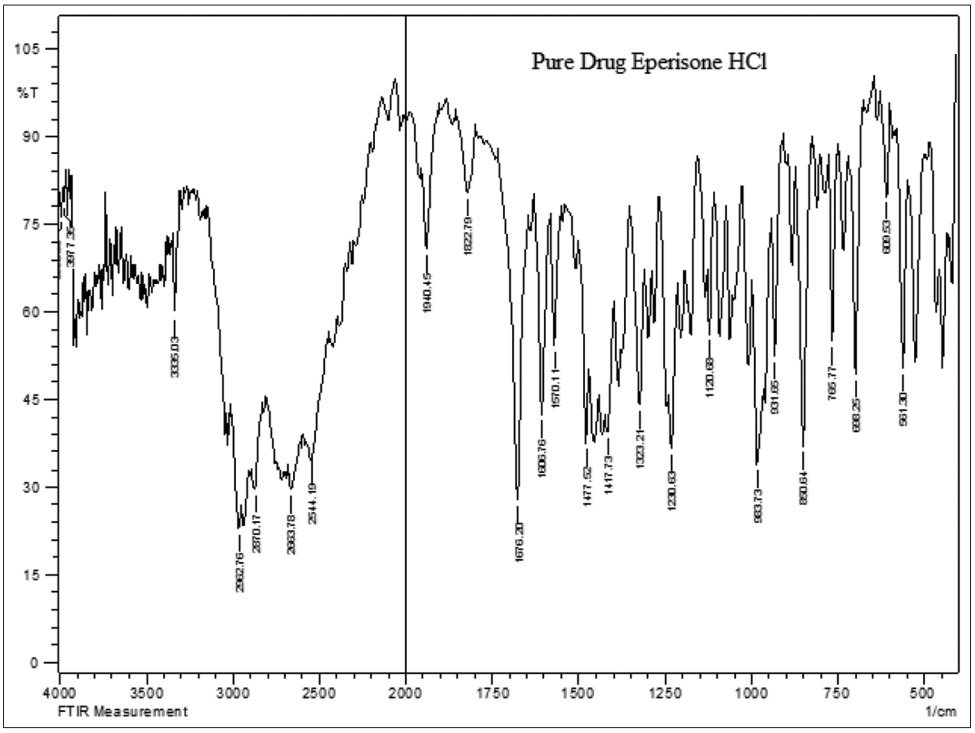

Figure 3: FT-IR spectra of Eperisone hydrochloride drug

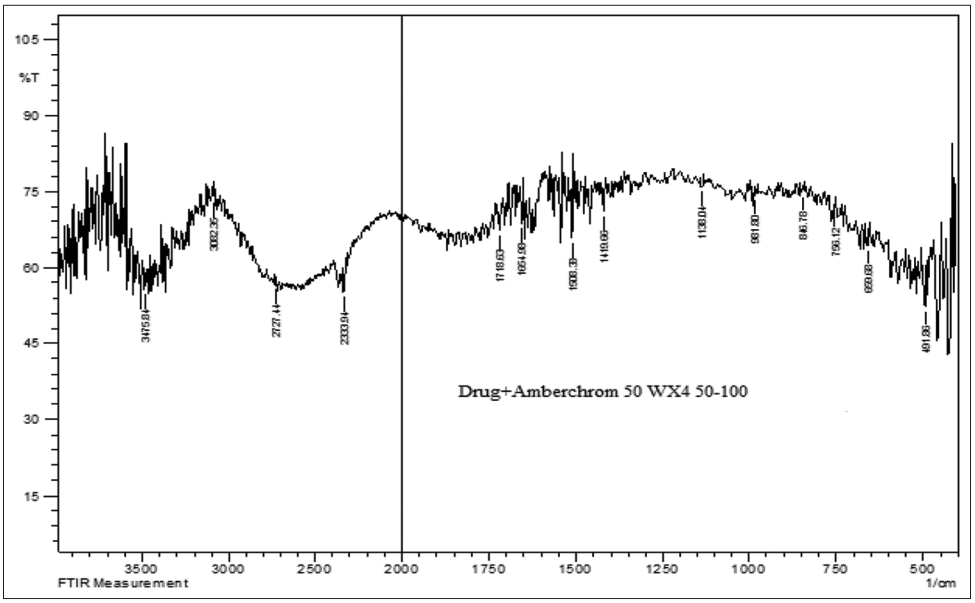

Figure 4: FT-IR spectra of Eperisone hydrochloride Drug + Amberchrom 50 WX4 50-100

Table 6: Data obtained for fourier transform infrared spectra of Eperisone hydrochloride along with ion exchange resins

Ingredients	*Principal peaks (cm^{-1})*					
	Functional groups					
	C-H Str (aromatic)	*C-HStr (aliphatic)*	*N-H*	*C-N*	*C=C*	*C-O*
Pure drug	3054.76	2663.78	3335.03	1230.63	1606.76	1120.68
Drug + amberchrom 50 w×4 50–100	3082.35	2727.44	3475.84	1256.40	1654.98	1138.04
Amberchrom 50 w×4 50–100	3066.68	2748.65	3462.34	1220.98	1635.69	1111.03
Amberchrom 50 w×8 100–200	3095.85	2736.38	3483.56	1213.27	1641.48	1037.74
Drug + amberchrom 50 w×8 100–200	2960.83	2675.36	3427.62	1289.18	1550.82	1051.98

Drug=Eperisone hydrochloride

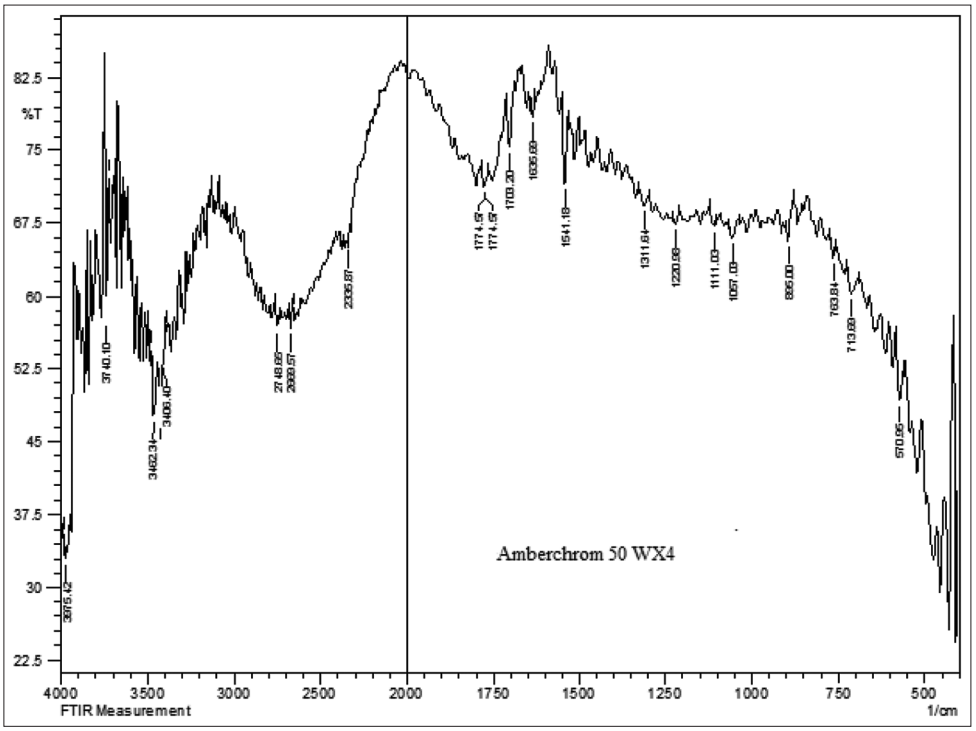

Figure 5: FT-IR spectra of Amberchrom 50 WX4 50-100

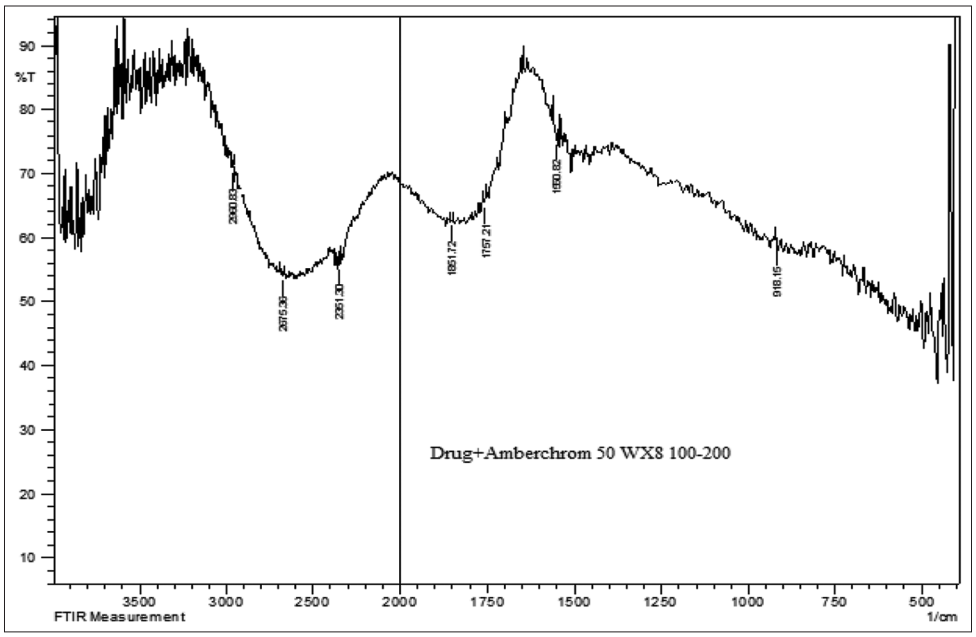

Figure 6: FT-IR spectra of Eperisone Hydrochloride + Amberchrom 50 WX8 100-200

Table 7: Evaluation of physical properties of cationic ion exchange resins

Ion exchange resins	*Average particle size (µm)*	*Water uptake time (s)*
Amberchrom 50 w×4 50–100	196.17	67±5
Amberchrom 50 w×4 100–200	111.9	55±5
Amberchrom 50 w×4 200–400	55.2	46±5
Amberchrom 50 w×8 100–200	108.5	53±5
Amberchrom 50 w×8 200–400	53.2	43±5

ratio were showed good acceptable range. The investigated results were given in Table 8.

Effect of resin activation on % drug complexation

To study the effect of pH of the activation medium of IER on percentage drug loading (single batch method), the resin were activated in the different pH environment (the result are reported

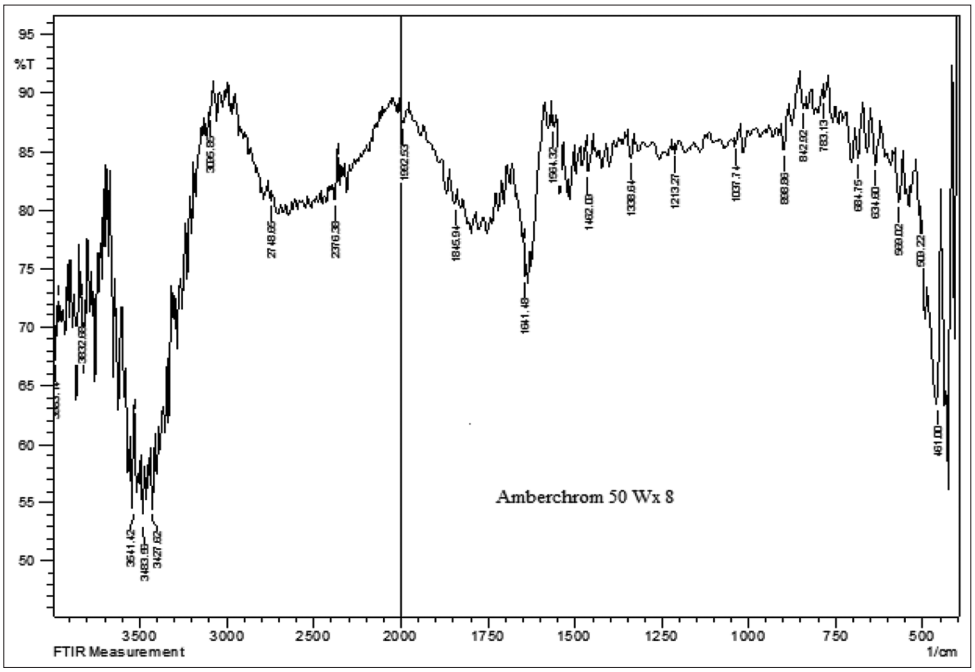

Figure 7: FT-IR spectra of Amberchrom 50 WX8 100-200

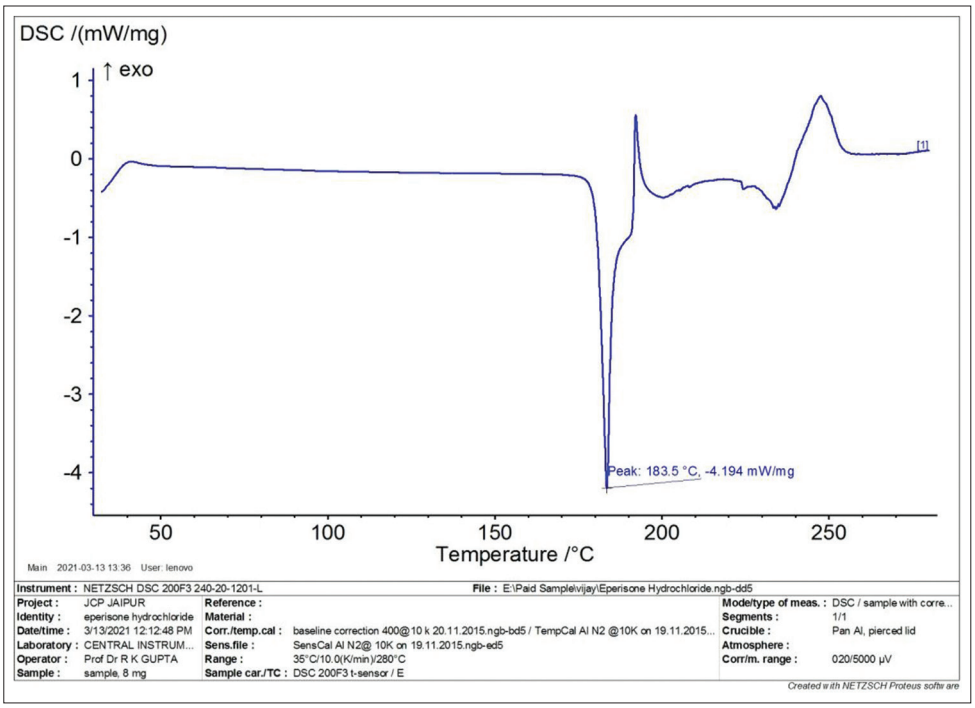

Figure 8: DSC thermogram of Eperisone hydrochloride

Table 8: Micromeritics properties of ion exchange resin

Ion exchange resins	*Bulk density*	*Tapped density*	*Carr's index*	*Hausner ratio*	*Angle of repose*
Amberchrom 50w×4 50–100	0.69	0.76	8.33	1.09	16.17
Amberchrom 50w×4 100–200	0.75	0.79	5.97	1.06	18.26
Amberchrom 50w×4 200–400	0.86	0.95	9.05	1.10	22.29
Amberchrom 50w×8 100–200	0.77	0.83	7.66	1.08	17.74
Amberchrom 50w×8 200–400	0.87	0.95	7.64	1.08	24.23

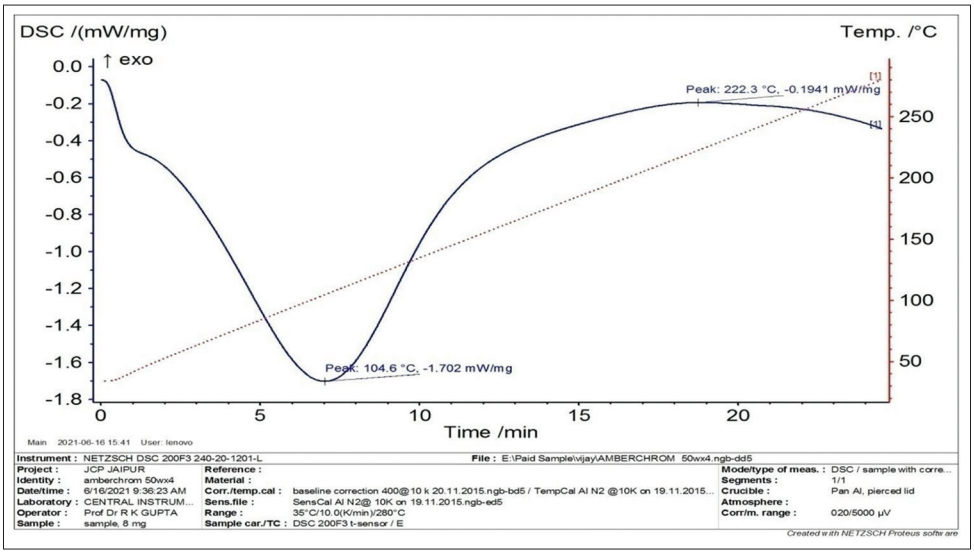

Figure 9: DSC thermogram of Amberchrom 50 WX4 50-100

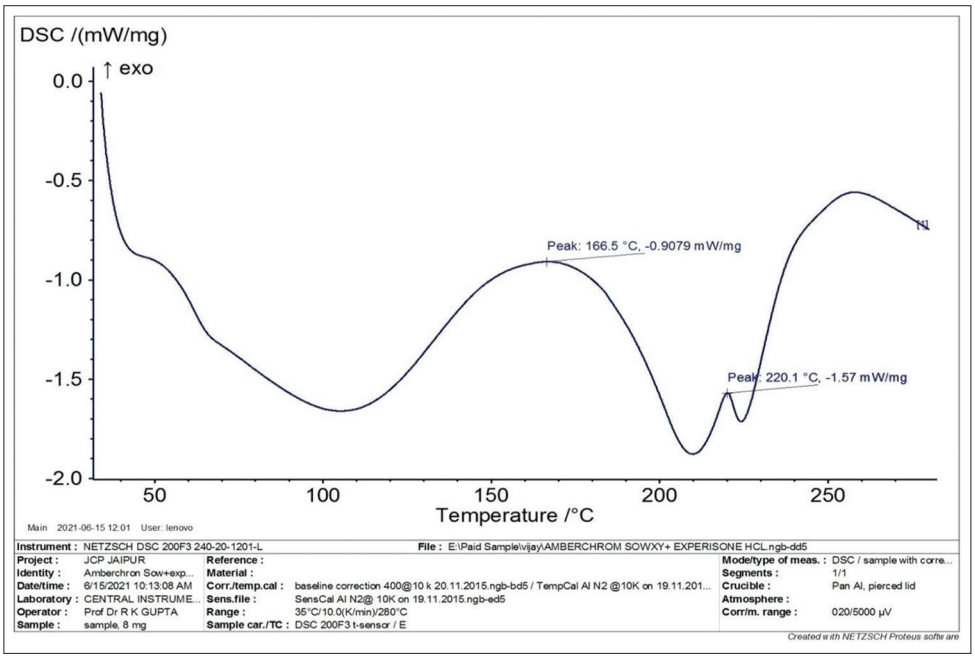

Figure 10: DSC thermogram of drug resin complex (Drug + Amberchrom 50 WX4 50-100)

Table 9: Effect of resin activation on percentage drug complexation

Resins	*Effect of resin activation on percentage drug complexation*			
	Inactivated	*Acid*	*Base*	*Acid + base*
Amberchrom 50 w×4 50–100	59.58	63.83	70.75	73.42
Amberchrom 50 w×4 100–200	54.66	57.17	59.42	62.42
Amberchrom 50 w×4 200–400	50.08	50.42	51.33	53.75
Amberchrom 50 w×8 100–200	54.50	57.58	59.33	60.75
Amberchrom 50 w×8 200–400	48.25	49.67	50.25	51.92

in Table 9 and Figure 11). It was found that highest drug loading was obtained in the resin treated with acid alkali combination. This study also revealed that highest complexation was achieved with Amberchrom 50 WX4 50–100 IER.

Effect of resin particle size and degree of cross linking on the loading equilibrium time

Resins of various particle sizes and degrees of cross linking were used to investigate their effect on the equilibrium time. The weight ratio between the drug and resin was 1:1 for the loading. Figure 12 shows the equilibrium profiles of drug loading onto different ion exchange resins. The loading of Eperisone hydrochloride in all the selected resins was more than 50%. The equilibrium time was approximately 120 min for Amberchrom 50wx4 50–100, 40 min for Amberchrom 50wx4 100–200 and 30 min for Amberchrom 50wx4 200–400, 50 min for Amberchrom 50wx8 100–200, and 40 min for Amberchrom 50wx8 200–400. The difference in equilibrium time obtained was due to the influence of the degree of cross-linking and the particle size of the resins. Amberchrom

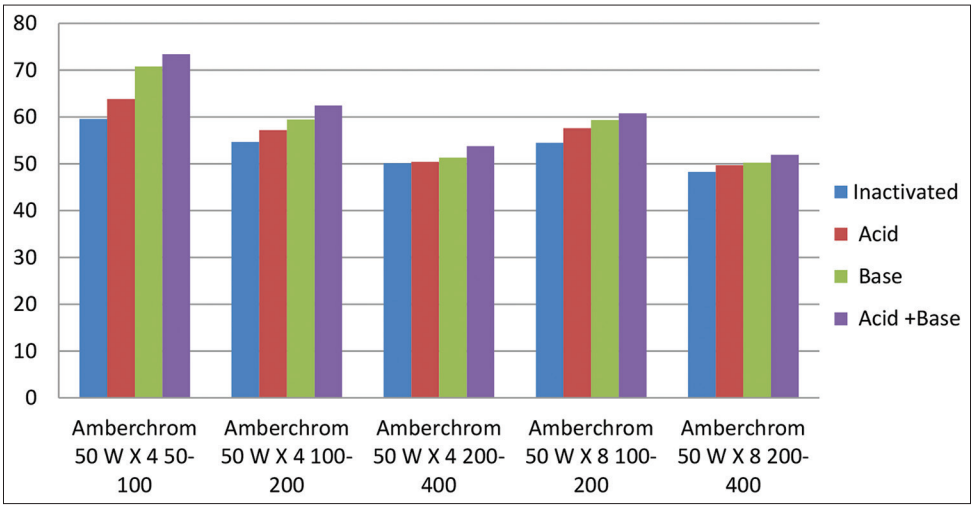

Figure 11: Effect of resin activation on % drug complexation

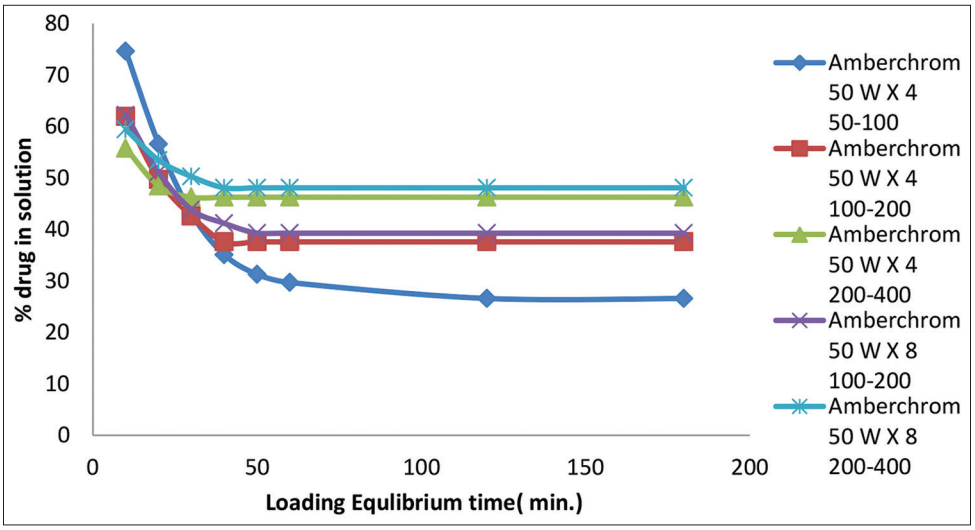

Figure 12: Equilibrium profile of drug loading onto different ion exchange resins

Table 10: Dissolution profile of different resinate

Drug resin complex	*Cumulative percentage drug release within time (min)*						
	30	*60*	*120*	*180*	*240*	*300*	*360*
Drug+amberchrom 50 wx 450–100	9	14.26	26.27	36.05	48.09	59.39	69.21
Drug+amberchrom 50 wx 4 100–200	14.25	26.27	39.04	50.34	60.89	72.21	82.04
Drug+amberchrom 50 wx 8 100–200	12.75	21.76	34.54	47.33	60.13	70.7	78.27
Drug+amberchrom 50 wx 4 200–400	18.75	29.27	40.55	53.35	67.66	80.48	90.32
Drug+amberchrom 50 wx 8 200–400	16.5	27.01	36.79	50.34	67.65	75.97	86.55

Table 11: Effect of resin particle size and degree of cross linking on the *in vitro* release of eperisone hydrochloride from drug resinate beads

Drug resin complex	*Average particle size (μm)*	*Cumulative percentage drug release*
Drug+amberchrom 50 wx4 50–100	196.17	69.21
Drug+amberchrom 50 wx 4 100–200	111.9	82.04
Drug+amberchrom 50 wx 8 100–200	108.5	78.27
Drug+amberchrom 50 wx 4 200–400	55.2	90.32
Drug+amberchrom 50 wx 8 200–400	53.2	86.55

50wx4 50–100 shows the largest particle size so it take more time for to reach equilibrium. Coarse particles have smaller surface area than fine particles and greater internal volume for ions to diffuse, so more time can be required to establish equilibrium. Resins with lower degree of cross linking reached equilibrium faster than resins with higher one having the same particle size. When an ion-exchange resin is highly cross linked, the diffusion of various ions can be impeded, and this will slightly increase the time required to reach equilibrium and reduce the amount of drug loaded onto IER.

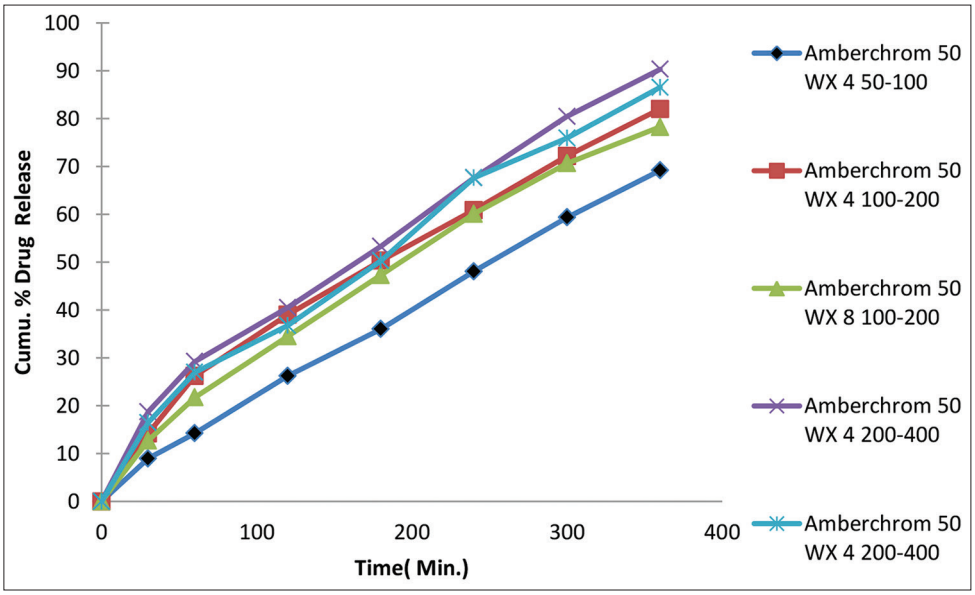

Figure 13: Effect of resin particle size and degree of cross linking on the *in vitro* release of EpeH from drug resinate beads

Table 12: *In vitro* release kinetics of drug from different resinate

Drug resin complex	*Zero order*		*First order*		*Higuchi*		*Korsemeyer peppas*	
	K_0	R_2	K_1	R_2	K_H	R_2	*n*	R_2
Drug + amberchrom 50 w×4 50–100	0.22	0.999	0.045	0.979	2.676	0.978	0.833	0.996
Drug + amberchrom 50 w×4 100–200	0.319	0.989	0.044	0.976	3.675	0.994	0.681	0.995
Drug + amberchrom 50 w×8 100–200	0.291	0.991	0.045	0.989	3.415	0.993	0.734	0.999
Drug + amberchrom 50 w×4 200–400	0.364	0.996	0.043	0.942	4.093	0.985	0.626	0.993
Drug + amberchrom 50 w×8 200–400	0.337	0.991	0.044	0.962	3.846	0.982	0.662	0.991

Effect of resin particle size and degree of cross linking on the in vitro release of EpeH from drug resinate beads

Fine particles have more surface area than coarse particles and less internal volume for ions to diffuse, so less time can be required to establish equilibrium. Similarly, desorption of bound drug from the complex will be faster in fine particles. Figure 13 shows the release profiles of EpeH from drug–resinate beads with different particle size resins (Amberchrom 50wx4 50–100 is 196.17 µm, Amberchrom 50wx4 100–200 is 111.90 µm, Amberchrom 50wx4 200–400 is 55.20 µm, Amberchrom 50wx8 100–200 is 108.50 µm, and Amberchrom 50wx8 200–400 is 53.20 µm). It is obvious that the higher degree of cross linking of resins, the slower the release of the drug. Statistical analysis revealed that EpeH–resinate with Drug + Amberchrom50wx4 200–400 showed significantly faster drug release (40.55, 67.66, and 90.32%), compared to EpeH–resinate with Drug + Amberchrom 50wx8 200–400 resinate (36.79, 67.65, and 86.55%) after 2, 4, and 6 h, respectively Dissolution data are given in Table 10. This may be attributed to the swelling properties of the resin. The higher degree of cross linking resins swell less than the lower ones, and hence is more resistant to diffusion of drug molecule throughout the resin particle. Results also showed in Table 11 that decreasing the particle size results in a faster drug release. This is attributed to the greater surface area exposed to the dissolution medium, which facilitates the exchange process.

Based on the above results, we decided to prepare drug resin microcapsules of EpeH that approach the zero-order kinetics for once daily administration and prevent burst release. The drug resin complex with Amberchrom 50wx4 50–100 was selected as highest drug binding of 73.42% and the desired slow release of drug was observed with resinate of drug with Amberchrom 50wx4 50–100 was selected to be microencapsulation to achieve the targeted controlled release effect.

Conclusion

The *in vitro* release kinetics as presented in Table 12 suggests that drug release from resinates of Amberchrom 50WX4 50–100, Amberchrom 50wx4 200–400, and Amberchrom 50wx 8 200–400 follows zero-order kinetics. These conclusions are based on co relation coefficient of linear relationship.

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