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Synthesis of an Ethylenediamine-Modified Hypercrosslinked Polymer and its Preliminary Study for Antipyrine and Pamabrom Extraction

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Emerging contaminants (EC) are naturally occurring or synthetic chemicals that may enter the environment and cause adverse effects to aquatic and human health. EC consist of pharmaceuticals, pesticides, organic chemicals and personal care products that present in water sources at low concentrations (μg/L), hence, they are not widely monitored in the environment. Pharmaceuticals contain biologically-active components that pollute water courses. These generally originate from human waste or the uncontrolled release of residues from chemical plants. The removal of pharmaceutical compounds from water can be carried out using polymeric materials with high specific surface areas and good selectivity due to the presence of accessible active functional groups. In the present work, the synthesis and characterizations of microspheres, acrylonitrile-co-divinylbenzene-80-co-vinylbenzylchloride(AN-co-DVB-80-co-VBC) terpolymers with weak-anion-exchange (WAX) character and high porosity have been successfully carried out. The polymeric microspheres were synthesized by precipitation polymerization and subsequently hypercrosslinked (HXL) via a Friedel-Crafts reaction. The HXL terpolymer was then chemically modified with 1,2-ethylenediamine (EDA) to incorporate diamine functional groups, which improved the selectivity of the HXL microspheres towards polar compounds. Fourier Transform-Infrared (FT-IR) spectra of the EDA-modified HXL terpolymer showed that the nitrile groups derived from AN units were utilized due to the presence of diamine groups along the polymeric chains, indicating that the chemical modification was successful. The microanalysis showed that the chlorine content of the polymer was significantly decreased after hypercrosslinking, indicating that the reaction was successful. The nitrogen content increased after chemical modification with EDA, indicating successful chemical modification of the microspheres. The polymers were in the form of spherical monodisperse polymer microspheres with mean particle diameters of ~7.00 μm. The highest observed specific surface areas (SSAs) of the HXL terpolymer and EDA-modified HXL terpolymer were 2,274 m^2/g and 503 m^2/g, respectively. The microspheres were utilized to extract the pharmaceutical compounds antipyrine and pamabrom from aqueous solution using the dispersive solid phase extraction (DSPE) method. The extraction analysis was carried out by Gas Chromatography–Mass Spectrometry (GC-MS). The influence of adsorbent dosage, extraction time and elution time were studied to evaluate the performance of the adsorbent in the extraction of antipyrine and pamabrom from aqueous solution. It can be concluded that EDA-modified HXL poly(AN-co-DVB-80-co-VBC) was more favourable towards the extraction of antipyrine, which had a maximum extraction efficiency (EE%) of 95%, compared to that of pamabrom (maximum EE% of 54%).

Key words: Dispersion-solid phase extraction; polar analytes; pharmaceuticals; polymerization; active functional group

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Emerging contaminants (EC), which include pharmaceuticals and personal care products (PPCPs), are constantly discharged into the environment in large quantities. Pharmaceuticals enter water systems

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primarily through two routes: improper disposal into water treatment systems and human excretion. Pharmaceutical residues have many physiochemical and biological properties that must be considered to predict their fate in the environment [1]. Pharmaceuticals are usually present in water at concentrations in the range of μg/L to ng/L, which are considered to be a potential threat to the environment [2]. Traces of pharmaceuticals have been detected in drinking water [2,3] and in cooked seafood [5] that may potentially risk the safety of consumers either through direct effects or indirectly through potential antimicrobial resistance [6]. Antipyrine and pamabrom are drugs commonly used by humans and widely produced as effluent waste in many industrial sectors [7]. Long term exposure to antipyrine can cause organ failure due to its toxicity towards mucosa and the lungs [8]. Pamabrom can cause genetic code damage, denaturation of proteins in cells and oxidative degradation of lipids in both aquatic and human life [9]. Rapid urbanization and industrialization near rivers and poor removal efficiencies in wastewater treatment plants (WWTPs) are the major reasons that have led to pharmaceutical pollution in aquatic life [10].

The analysis of pharmaceutical pollutants can be very challenging due to their trace level concentration range (down to few ng/L) as well as the fact that they usually exist in environmental samples as a complex mixture of pollutants from different chemical classes. Hence, the analytical method used for pharmaceutical residues in environmental matrices must be highly sensitive and selective to enhance the extraction of targeted polar analytes in water matrices [7,8]. Solid phase extraction (SPE) is the best technique currently available for rapid and selective sample preparation in the analysis of pharmaceuticals. SPE has many advantages over traditional techniques such as liquid-liquid extraction (LLE), such as facility of operation, high recoveries of analyte, easy handling, better ability to extract analytes of wide polarity range and lower consumption of solvents [9,10]. Generally, SPE technology must be utilized in combination with instrumental analysis, and of these, gas chromatography-mass spectrometry (GC-MS) is the preferred method for separation and quantification of polar analytes. For instance, Ballesteros et al. successfully separated endocrine disrupting compounds (EDCs) in environmental water using an SPE system in combination with GC-MS [15]. The detection of phenazone, a non-steroidal anti-inflammatory drug (NSAID) was also carried out using SPE with GC-MS extraction analysis, and the results showed that phenazone was detected in the raw water samples at up to 2.5 μg/L [16]. However, SPE suffers from several drawbacks, such as difficulty in performing simultaneous extractions, cartridge blocking, and the potential for a prolonged procedure duration [17].

In this case, a simple and rapid extraction procedure termed dispersive solid phase extraction (DSPE) was introduced as an alternative to the conventional SPE method to reduce the sample clean-up time. A unique and attractive property of the DSPE procedure is that a small amount of polymer microspheres is directly dispersed in a sample solution to remove the matrix interferences *via* centrifugation and filtration. The target analytes are selectively retained onto the sorbent that is later removed, while the supernatant is subjected to the rest of the analytical process. The analytes are later desorbed from the sorbents with an appropriate polar solvent before being detected and analyzed *via* GC-MS. DSPE is performed using the same methodology as SPE; the only difference is the sorbents are directly added into the extract without a conditioning step. Moreover, DSPE can enhance extraction efficiency by increasing the contact between analytes and the sorbents [18]. Matsuta et al., for example, separated and enriched 13 analytes in blood using a modified DSPE "QuEChERS" method by adding a mixture of magnesium sulphate, sodium chloride and acetonitrile into whole blood. The solution was then shaken intensively and centrifuged before mixing the adsorbent (graphitized carbon Envi-carb) with magnesium sulfate. After centrifuging, almost all the impurities in the blood matrix were removed and the suspension was cleaned by the way of DSPE and transferred to autosampler vials for analysis by GC-MS. The recoveries of the analytes spiked into whole blood are in the range of 59% to 93% with the limit of detection at 0.5 μg/mL [19]. Further, Fagerquist et al. utilized a novel, rapid, sensitive DSPE coupled with LC/MS/MS for detection of 10 â-lactam antibiotics in bovine kidney tissues. All the recoveries of antibiotics were above 70% (apart from desfuroylceftiofur cysteine disulfide (DCCD), with a recovery of 58%). Compared to conventional SPE, the proposed method could handle 3-4 times the number of samples in one day, and could also be used for quicker pre-treatment of samples [20].

The selection of a sorbent is a critical step in DSPE, and it is important to consider the physiochemical properties that allow maximal interaction between the sorbent and the analytes. As a consequence, an ideal sorbent should not only reduce the consumption time, but also enhance the extraction selectivity, removal, or preconcentration of the analytes present in an analytical matrix [21]. There are various sorbents available for use in SPE, such as carbonaceous materials and bonded-phase silica, but generally polymeric resins are the best-suited polymeric adsorbents due to their high specific surface area, monodispersity, high adsorption capacity and the ion-exchange characteristics in the polymer particles that give better selectivity [18,19]. These materials have hydrophilic, hydrophobic, or π–π interactions that allow the effective extraction of acidic, neutral, or basic compounds over a wide pH range. Many studies on ion-exchange resin-based SPE technology have been published in the literature. Fontanals and co-

workers prepared eight different strong cation-exchange (SCX) resins by utilizing precipitation polymerization (PP) or non-aqueous dispersion polymerization methods. HXLPP-SCX resins, which are considered as adsorption extractants, are used in SPE to monitor pharmaceutical compounds in wastewater samples. The results indicated that these kinds of SCX adsorbents are equipped with higher ion-exchange abilities and high specific surface areas [24]. Similar studies on SCX-type sorbents were also reported by Fontanals et al., in which two alkyl sulfate reagents were synthesized using two different methods, copolymerization and chemical modification with sulfonic groups through a post-hypercrosslinking reaction. All polymers were in the form of microspheres (with mean particle diameters of 3-5 μm) with specific surface areas up to 1370 $m^2.g^{-1}$. The two materials were used as SPE sorbents for the extraction of cationic species from real water samples [25].

The procedure used to generate the HXLPP-SCX sorbent was also used to prepare a hypercrosslinked sorbent, which was further modified with 5% or 10% dimethylbutylamine (DMBA). This generated strong anion-exchange (SAX) resins with two ion-exchange capacities (IECs) (0.2 and 0.4 $meq.g^{-1}$, respectively) and specific surface areas of about 1000 $m^2.g^{-1}$. These properties of the HXLPP-SAX sorbents are better than those of commercial sorbents, which indicates that HXLPP-SAX are promising materials for future work in this area. When the HXLPP-SAX sorbent was applied to the SPE of environmental water samples, the results showed quantitative and selective extraction of low levels of acidic pharmaceuticals from 500 mL of river water and 100 mL of effluent wastewater [26]. The vinylbenzyl chloride-divinylbenzene (VBC-DVB) precursors were prepared using the PP method followed by a hypercrosslinking reaction which was then modified with piperazine and 1,2-ethylendiamine (EDA) moieties to generate hypercrosslinked resins with weak anion-exchange (WAX) characteristics [27]. An added feature of HXLPP-WAX sorbents is that they were synthesized as monodisperse and low-micron-sized particles (~5 μm), which are suitably shaped for SPE packing columns. A group of acidic pharmaceuticals was selectively extracted from complex environmental water samples after effective clean up involving 1 mL of methanol, which also provided clean chromatograms on liquid chromatography (LC) analysis [27]. Lakade et al. developed a new extraction material, namely hypercrosslinked Q-100 magnetic particles, which was tested in DSPE for a group of sweeteners from environmental samples. Under optimum conditions, Q-100 showed suitable extraction recovery of river water samples, ranging from 21% to 88% for all the sweeteners, except for alitame (12%). The validated method based on DSPE using Q-100 followed by LC-tandem MS provided good linearity and limits of quantification between 0.01 and 0.1 μg/L. This method was used to analyse samples from river water and wastewater, and four sweeteners (acesulfame, saccharin, cyclamate, and sucralose) were found in both types of samples [28]. Typically, a polymeric sorbent possesses good adsorption capability and high retention of polar analytes, thus when an appropriate one is selected, good results will be achieved.

In this study, EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) polymeric particles (**Figure 1**) were used as an adsorbent in DSPE for the extraction and analysis of two selected analgesic drugs (antipyrine and pamabrom) in aqueous solution. Antipyrine (pKa = 1.4) and pamabrom (pKa = 0.23) were selected as target analytes as they are the most commonly used analgesic drugs that exist at ng/L levels in water sources [19,20]. EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) was synthesized and used as a DSPE sorbent followed by analytical determination by GC-MS. A preliminary study was carried out to evaluate the ability of the adsorbents to extract antipyrine and pamabrom from aqueous solution.

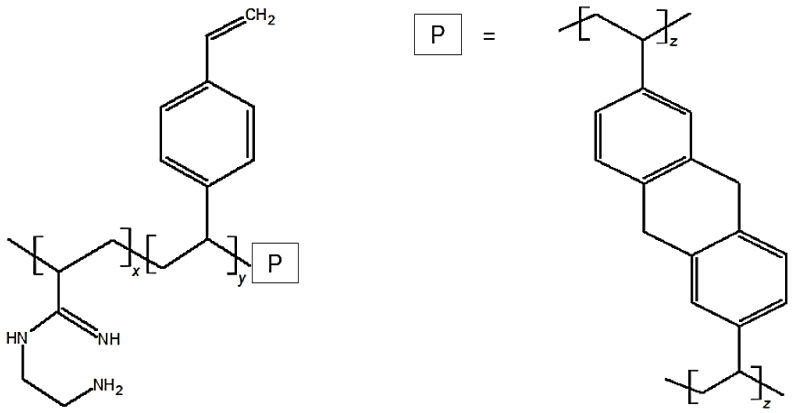


Figure 1. Molecular structure of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC).

*P is the HXL poly(AN-*co*-DVB-80-*co*-VBC).

Table 1. Monomers in the feed mixture of acetonitrile and toluene for the synthesis of poly(AN/DVB-80/VBC)

Samples code	Mol ratio, %			Volume, mL		
	AN	DVB-80	VBC	AN	DVB-80	VBC
A8	35	60	5	0.879	3.277	0.270
A9	40	55	5	1.043	3.119	0.281

EXPERIMENTAL

1. Reagents and Materials

The reagents used for polymer synthesis were acrylonitrile (AN) of ≥99 % purity (Merck, Netherlands), divinylbenzene-80 (DVB-80) (80 % grade) and vinylbenzyl chloride (VBC) (95% grade). DVB-80 and VBC were both supplied by Sigma-Aldrich (Dorset, UK). AN, DVB-80 and VBC were freshly purified prior to the synthesis by passing them through a short column of neutral alumina to remove inhibitors. Benzoyl peroxide (BPO), which acts as an initiator in the precipitation polymerization, was supplied by Sigma-Aldrich (Dorset, UK). This was further purified *via* recrystallization by acetone (≥99 % grade) and washed with cold acetone. Acetonitrile (HPLC grade), toluene (≥99 % grade), methanol (≥99 % grade) and acetone which were used as the medium for precipitation polymerization were all supplied by Sigma-Aldrich (Dorset, UK). 1,2-dichloroethane (DCE) (≥99 % grade) (Sigma-Aldrich, Dorset, UK) and iron (III) chloride (Fisher, US) were used as reagents for the hypercrosslinking reaction. Ethylenediamine (≥99 % grade) was supplied by Sigma-Aldrich (Dorset, UK). Antipyrine and pamabrom were supplied by Sigma-Aldrich (Dorset, UK). All other reagents were used as received.

2. Precipitation Polymerisation of Poly(AN/DVB-80/VBC)

DVB-80 (0.60 mol), VBC (0.05 mol) and AN (0.35 mol) were added to a Nalgene® plastic bottle. BPO and a mixture of acetonitrile and toluene were then added. The bottle was lightly sealed with Parafilm and placed in an ultrasonic bath for 10 min. After this, the bottle was placed on an ice bath and deoxygenated by sparging with nitrogen gas for 30 min. After resealing, the bottle was placed on a low-profile roller and rotated slowly, spinning about its long axis at 10 rpm. The temperature of the incubator was increased from ambient to 60 ˚C over a period of approximately 2 h. Polymerisation was allowed to occur for 94 h after the incubator reached 60 ˚C. After the 96 h period, the milky suspension of polymer particles was filtered using a 0.20 µm nylon membrane and washed with 20.00 mL each of acetonitrile, toluene, methanol and acetone. After washing, the polymer sample was dried overnight in a vacuum oven at 40 ˚C (ref). The monomers used in the feed mixture of acetonitrile and toluene for the synthesis of poly(AN/DVB-80/VBC) were tabulated in **Table 1**.

3. Hypercrosslinking Reactions

The terpolymer particles (1.00 g) and 30.00 mL of DCE were placed in a round-bottomed flask and the mixture was placed under nitrogen for 1 h. Then, $FeCl_3$ suspended in DCE was added. The mixture was heated rapidly to 80 ˚C and kept at this temperature for 18 h. The hypercrosslinked particles were filtered and washed, first with methanol, and then several times with aqueous HNO_3 (pH 1). Next, the particles were extracted overnight with acetone in a Soxhlet extractor and washed again with methanol and diethyl ether before drying to constant mass in a vacuum oven at 40 ˚C overnight [31].

4. Preparation of EDA-HXL-AN/DVB-80/VBC Particles

EDA-modified hypercrosslinked (HXL) poly(AN-*co*-DVB-80-*co*-VBC) (mol ratio: 35/60/5 and 40/55/5) was chemically prepared by following previously reported procedures [22]. Briefly, 0.5 g of HXL terpolymer was weighed and added to 40 mL of 1,2-dichloroethane (DCE) in a 100 mL three-neck round-bottom flask with a magnetic stirrer. Then, the solution mixture was purged with nitrogen gas for 4 h so that the beads swelled. Then, 10% excess of ethylenediamine (EDA) was added to the mixture which was heated at 88 °C for 24 h. The resultant solid was filtered and washed with toluene, methanol and distilled water. Finally, the EDA-modified HXL terpolymer particles were dried overnight in a vacuum oven at 40 °C.

5. Characterization of EDA-HXL-AN/DVB-80/VBC

AN/DVB-80/VBC, HXL AN/DVB-80/VBC and EDA-HXL-AN/DVB-80/VBC particles were characterized by Fourier Transform Infrared (FTIR) spectroscopy, elemental microanalysis, Brunauer-Emmett-Teller (BET) surface area analysis and scanning electron microscopy-energy dispersive X-ray (SEM-EDX) analysis. FTIR spectroscopy was carried out on a BX Perkin Elmer (United States) using the Universal Attenuated Total Reflectance (UATR) technique, and spectra were recorded in the range of 280-4000 cm^{-1}. The percentages of carbon,

hydrogen, and nitrogen compounds were determined using a Perkin Elmer 628 Series Instrument. The nitrogen sorption analysis was carried out at 77K on a Micrometrics ASAP 2010 (USA) surface area analyzer. Samples were degassed overnight at 100 °C and analyzed with a computer-controlled Module ASAP 2010 Version 2.00. The specific surface areas were determined from the linear part of the BET equation. SEM images were scanned using a JEOL JSM 6360LA (Tokyo, Japan). The particles were fixed on the steel stub with double-sided tape and then coated with platinum before scanning. The microsphere diameters and particle size distributions were calculated with ImageJ software using SEM images taken of 100 individual particles. EDX analysis was equipped with SEM in order to determine the chlorine content in the terpolymer before and after the hypercrosslinking reaction.

6. Sample Preparation

Stock standard solutions of antipyrine and pamabrom (200 ppm) were prepared by separately dissolving 20 mg of each drug in 100 mL of methanol.

7. Dispersive-Solid Phase Extraction (d-SPE) Procedure

5 mg of each adsorbent (AN/DVB-80/VBC, HXL AN/DVB-80/VBC and EDA-HXL-AN/DVB-80/VBC was added into 25 mL centrifuge tubes. Then, 10 mL of each drug solution (antipyrine and pamabrom) was added into the centrifuge tubes. The mixtures were centrifuged (4800 rpm) for 8 mins at 25 °C to promote sorption of analytes and facilitate the separation process between the adsorbents and the aqueous phase. After centrifugation was complete, the sample solutions were decanted, leaving the terpolymer particles in the centrifuge tubes. The polymer particles were allowed to dry for 30 mins before adding 10 mL of methanol into the centrifuge tubes to elute the polar analytes from the terpolymers. The mixtures were sonicated for 5 mins at 25 °C to promote the elution process. Finally, the supernatants were collected by micropipette and transferred into 2 mL vials for GC-MS analysis. The same procedures were applied by varying the amount of adsorbent (10, 15, 20, 25 and 50 mg), extraction time (10, 20, 30, 40, 50 and 60 mins) and elution time (3, 5, 10, 15 and 20 mins) in 10 mL of methanol (elution solvent). Extraction efficiencies (EE%) of polar analytes onto the polymeric adsorbent were calculated using Equation 1:

$$EE\% = \frac{Final\ concentration\ (C_f)}{Initial\ concentration\ (C_i)} \times 100 \qquad \text{(Equation 1)}$$

8. GC-MS Conditions

GC-MS analyses of the stock solutions and extracted samples were carried out on a Shimadzu QP2010 Plus (Kyoto, Japan) GC-MS with splitless injection at 330 °C, using an injection volume of 1 µL. Separations were carried out using a polar column (ZEBRON ZB5ms, 30-metre x 0.25 mm I.D x 0.25 µm film thickness). The carrier gas used was helium (purity 99.99%), supplied by Malaysian Oxygen (MOX) (Selangor, Malaysia), while the flow rate was set to 6.0 mL/min with a hold time of 3 min. The column oven temperature was held at an initial temperature of 70 °C for 3 min. Then, it was raised to 230 °C at 20 °C/min and held at 230 °C for 5 min. The total run time was 10 min. A mass range of *m/z* 50-320 was scanned to confirm the retention time of the analytes.

RESULTS AND DISCUSSION

1. Preparation and Characterization of EDA-HXL-AN/DVB-80/VBC

In this study, a precipitation polymerization method was used for the synthesis of poly(AN-*co*-DVB-80-*co*-VBC), a terpolymer precursor. It was observed that the initially homogenous solution of monomers and initiator became a cloudy, white suspension of particles after 48 h. Poly(AN-*co*-DVB-80-*co*-VBC) terpolymer was then hypercrosslinked (HXL) to develop a highly porous terpolymer system. The chemical modification of HXL poly(AN-*co*-DVB-80-*co*-VBC) with ethylenediamine (EDA) lead to the formation of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) (EDA-HXL-AN/DVB-80/VBC) with enhanced selectivity for the polar analytes antipyrine and pamabrom.

FTIR spectroscopy was employed to confirm the presence of diamine moieties integrated onto HXL-AN/DVB-80/VBC in the terpolymer system. **Figures 2(a)** and **2(c)** show the FT-IR spectra of poly(AN-*co*-DVB-80-*co*-VBC) for the AN/DVB-80/VBC mole fractions of (35/60/5) (A8) and (40/55/5) (A9), respectively. Based on the spectra in **Figures 2(a)** and **2(c)**, it can be confirmed that the precipitation polymerization was successful for all mole fractions of AN/DVB-80/VBC. This can be supported by the presence of the absorption band of an imine group (-C=N), C=C stretching in the aromatic ring, and the chloromethyl -CH_2Cl at 1444 cm^{-1}, 1600 cm^{-1} and 1267-1269 cm^{-1}, respectively, which confirm the incorporation of AN, DVB-80 and VBC in the terpolymer system. FT-IR spectra of HXL poly(AN-*co*-DVB-80-*co*-VBC) for mole fractions (35/60/5) (HA8) and (40/55/5) (HA9) were shown in **Figures 2(b)** and **2(d)**, respectively. After the hypercrosslinking reaction, the chloromethyl peak at ~1267 cm^{-1} was less intense and almost negligible compared to the absorption band before the HXL reaction (**Figure 2(b)** and **2(d)**). This suggests that chlorine was consumed in the Friedel-Crafts alkylation reaction and rigid methylene crosslinking bridges were created between benzene rings [32]. It can be confirmed that the HXL reaction that involved nucleophilic substitution was successfully carried out for all mole fractions of (AN/DVB-80/VBC) as the IR absorption band of chloromethyl was insignificant.

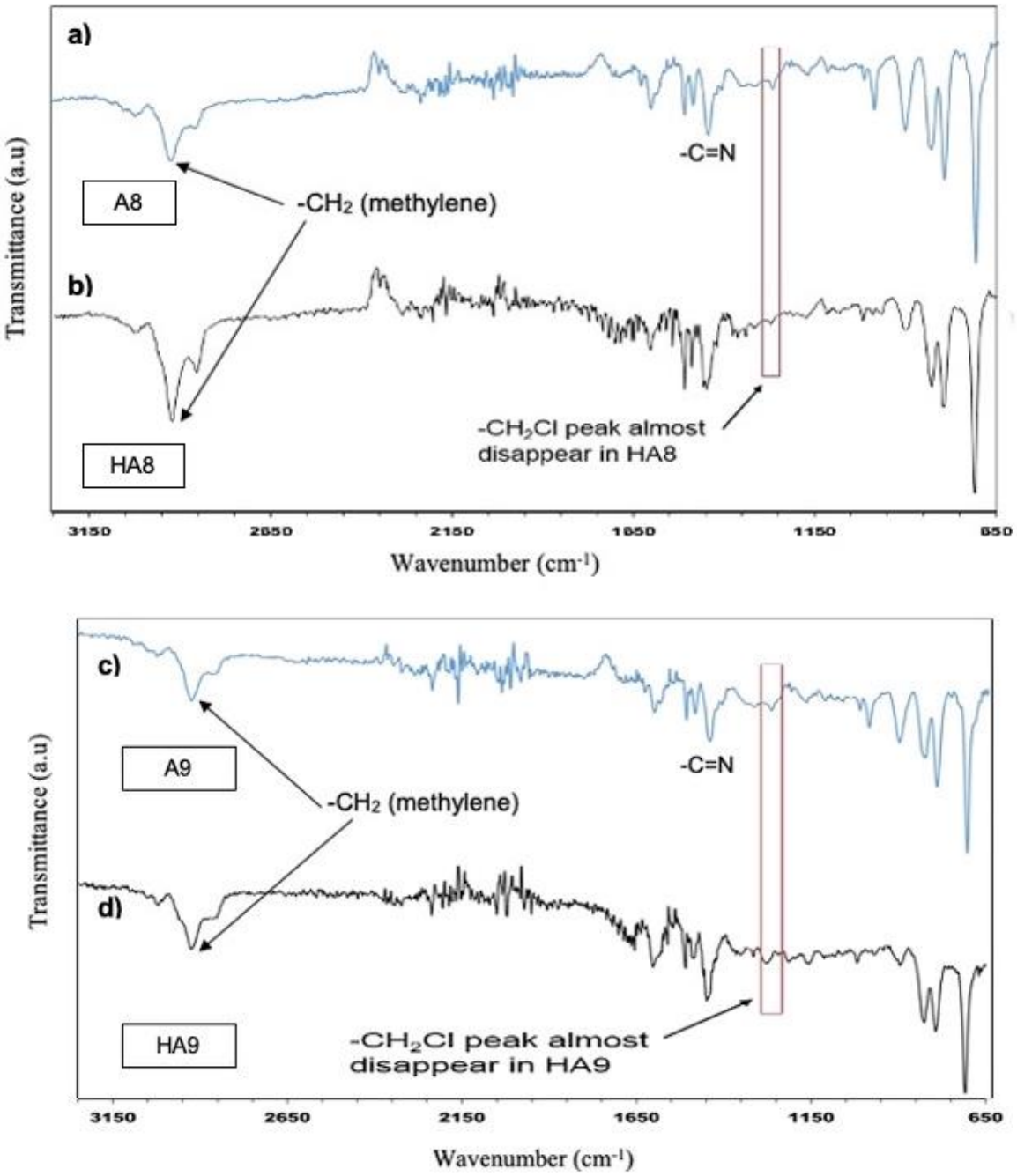


Figure 2. FTIR spectra of (a) AN-DVB-80-VBC (35/60/5) (A8), (b) HXL AN-DVB-80-VBC (35/60/5) (HA8), (c) AN-DVB-80-VBC (40/55/5) (A9), and (d) HXL AN-DVB-80-VBC (40/55/5) (HA9).

Figure 3 shows the FTIR spectra of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) for mole fractions (AN/DVB-80/VBC) of (35/60/5) (MHA8) and (40/55/5) (MHA9), respectively. The wide absorption band at ~3379-3381 cm^{-1} corresponds to the N-H stretching that belongs to the -NH and -NH_2 of ethylenediamine (EDA) [18,29]. The appearance of an absorption band which corresponds to the N-H stretching indicates that the chemical modification of HXL poly(AN-*co*-DVB-80-*co*-VBC) with EDA was successfully carried out due to incorporation of EDA at the nitrile group of poly(AN). Furthermore, the intensity of the band that corresponds to the chloromethyl pendant peak at ~1267 cm^{-1} was further weakened after the chemical modification reaction [32]. The absorption peak at ~1448 cm^{-1} belonging to the imine group, -C=N, was still present after chemical modification with ethylenediamine (EDA), representing the acrylonitrile functional group.

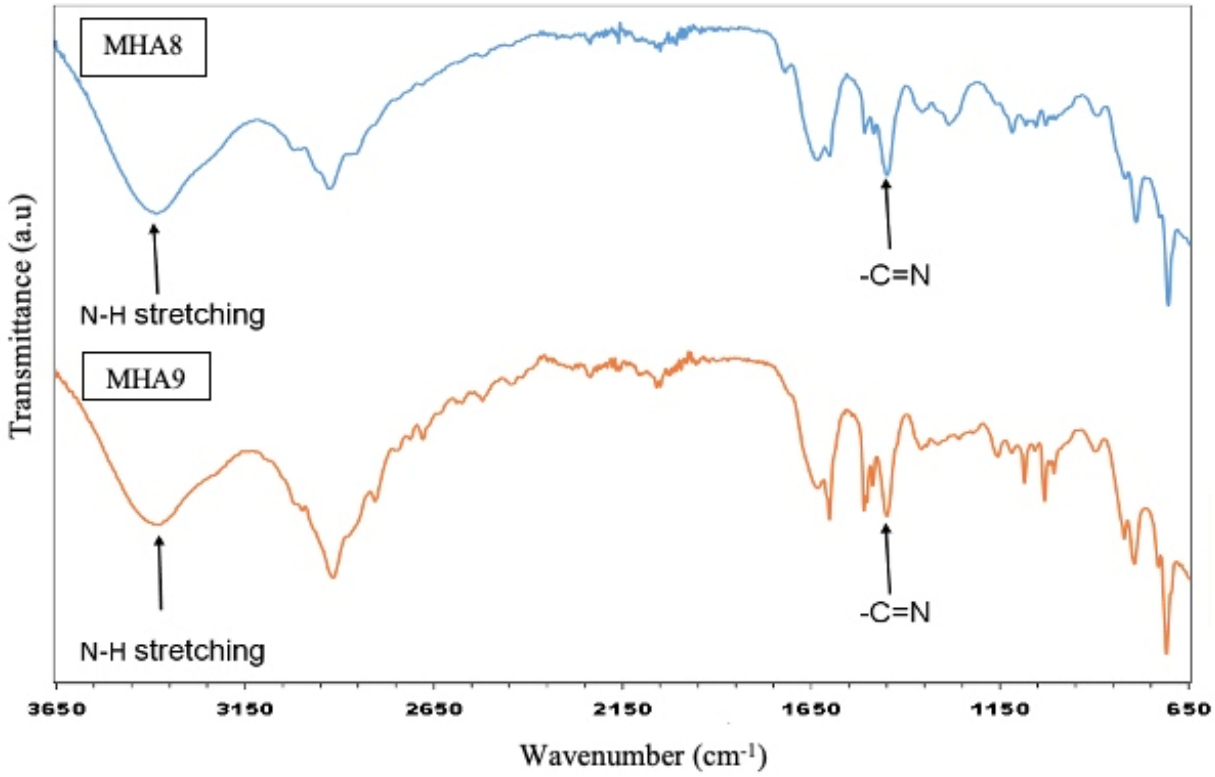


Figure 3. FT-IR spectra of EDA-HXL AN-DVB-80-VBC for mole fractions (35/60/5) (MHA8) and (40/55/5) (MHA9), respectively.

Elemental microanalysis was carried out to determine the percentage of carbon (C), hydrogen (H) and nitrogen (N) elements in the samples. **Table 2** shows the percentage of C, H and N for each mole fraction of poly(AN-*co*-DVB-80-*co*-VBC), HXL poly(AN-*co*-DVB-80-*co*-VBC) and EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC). The nitrogen content of HA8 and HA9 were 3.2% and 2.4% respectively, and these increased to 3.8% (MHA8) and 7.8% (MHA9) after chemical modification with ethylenediamine. This was due to the incorporation of two amino groups from EDA into the terpolymer system. However, since HA9 consisted of 55 mol% of DVB-80 while HA8 consisted of 60 mol% of DVB-80, it was expected that the lower amount of DVB-80 in HA9 made the polymer backbone less resistant to chemical modification with EDA. Hence, a higher amount of N was observed for MHA9. This supports the findings from the FTIR spectra of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) which show the presence of an N-H stretching band at ~3379 cm^{-1} after chemical modification.

Table 2. Elemental microanalysis data of poly(AN-*co*-DVB-80-*co*-VBC) and HXL poly(AN-*co*-DVB-80-*co*-VBC) and EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) terpolymers

Samples	AN/DVB-80/VBC, mol%	Elemental microanalysis, %		
		Carbon (C)	Hydrogen (H)	Nitrogen (N)
A8	35/60/5	83.2	7.3	3.4
HA8		81.3	7.0	3.2
MHA8		68.8	7.5	3.8
A9	40/55/5	83.7	7.2	3.2
HA9		82.8	8.7	2.4
MHA9		58.3	9.5	7.8

Table 3. BET data of poly(AN-*co*-DVB-80-*co*-VBC), HXL poly(AN-*co*-DVB-80-*co*-VBC) and EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) terpolymers

Samples	AN/DVB-80/VBC, mol%	Specific surface area, m^2/g	Specific pore volume, cm^3/g	Mean pore size, nm
A8		4	0.295	4.8
HA8	35/60/5	2274	0.955	3.5
MHA8		503	2.664	4.7
A9		2	0.033	4.8
HA9	40/55/5	1759	0.778	3.6
MHA9		53	0.699	5.0

The structural properties of the terpolymer particles were examined under nitrogen sorption analysis and these data are presented in **Table 3**. The BET surface areas of poly(AN-*co*-DVB-80-*co*-VBC) significantly increased from 4 m^2/g (A8) and 1.8 m^2/g (A9) to 2274 m^2/g (HA8) and 1759 m^2/g (HA9), respectively, after the hypercrosslinking reaction. The specific pore volumes also increased in the range of 0.295-0.955 cm^3/g, while the mean pore sizes were in the range of ~4.5 nm for all polymers. The significant increase in BET surface areas indicate that methylene bridges were formed in large amounts due to the chlorine consumption via a Friedel-Crafts reaction [27,29]. It is interesting to note that the HXL poly(AN-*co*-DVB-80-*co*-VBC) synthesized in this study has a higher BET surface area at 2274 m^2/g than previously studied HXL terpolymers with other comonomers. For instance, the BET surface area of HXL polystyrene(ST)-*co*-VBC-*co*-DVB-80) [35] and HXL poly(N-vinylimidazole(VIM)-*co*-VBC-*co*-DVB-80) [36] were 1161 m^2/g and 1306 m^2/g, respectively. However, after chemical modification with EDA, the BET surface area of HXL poly(AN-*co*-DVB-80-*co*-VBC) decreased to 503 m^2/g and 53 m^2/g for MHA8 and MHA9, respectively. This may be attributed to the amino groups on the HXL poly(AN-*co*-DVB-80-*co*-VBC) partially covering the pores on the surface of the terpolymer [33].

The SEM images of all terpolymer samples, namely A8, HA8, MHA8, A9, HA9, and MHA9 are presented in **Figure 4(a-f)**. Based on **Figure 4(a)**, the terpolymer particles of A8 were in the form of spherical beads, and the morphologies of the polymers (**Figure 4(b)**) were still retained through the hypercrosslinking reaction. As shown in **Figure 4(c)**, the EDA-modified HXL terpolymer microspheres were also still in the form of spherical beads. However, all polymers with the mole fraction (40/55/5) appeared in the form of agglomerations of small particles as shown in **Figure 4(d-f)**. This might be due to the low percentage (55%) of crosslinked monomers in DVB-80 monomer feed. A higher percentage of DVB-80 is required in order to produce spherical polymer microspheres[37].

As tabulated in **Table 4**, the mean particle diameters of poly(AN-*co*-DVB-80-*co*-VBC) (A8), HXL poly(AN-*co*-DVB-80-*co*-VBC) (HA8) and EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) (MHA8) were similar to one another, at ~7.0 μm, even after the modification reaction. The C_v values of A8, HA8 and MHA8 indicated that all terpolymers were monodisperse (C_v value below 15 %) [38]. Monodispersed particles have constant particle sizes and diameters which makes them very suitable for use in packed columns or as SPE polymeric adsorbents.

The chlorine content in the poly(AN-*co*-DVB-80-*co*-VBC) before and after HXL reaction was determined using energy dispersive x-ray (EDX) analysis in conjunction with SEM morphology analysis. **Table 5** shows that the chlorine content of poly(AN-*co*-DVB-80-*co*-VBC) for mole fractions (35/60/5) (A8) and (40/55/5) (A9) decreased to 0.61 and 0.92 wt%, respectively. After the HXL reaction, the chlorine content of HA8 and HA9 were reduced by 37% and 44%, respectively. Therefore, this result agrees with the FTIR spectra in which the chloromethyl absorption peak at ~1267 cm^{-1} was negligible after the HXL reaction, indicating the HXL reaction was successfully carried out. The lowest chlorine content was achieved by HA8 at 0.61 wt% which corresponds to the highest BET surface area (2274 m^2/g) among all the different mole fractions of HXL poly(AN-*co*-DVB-80-*co*-VBC).

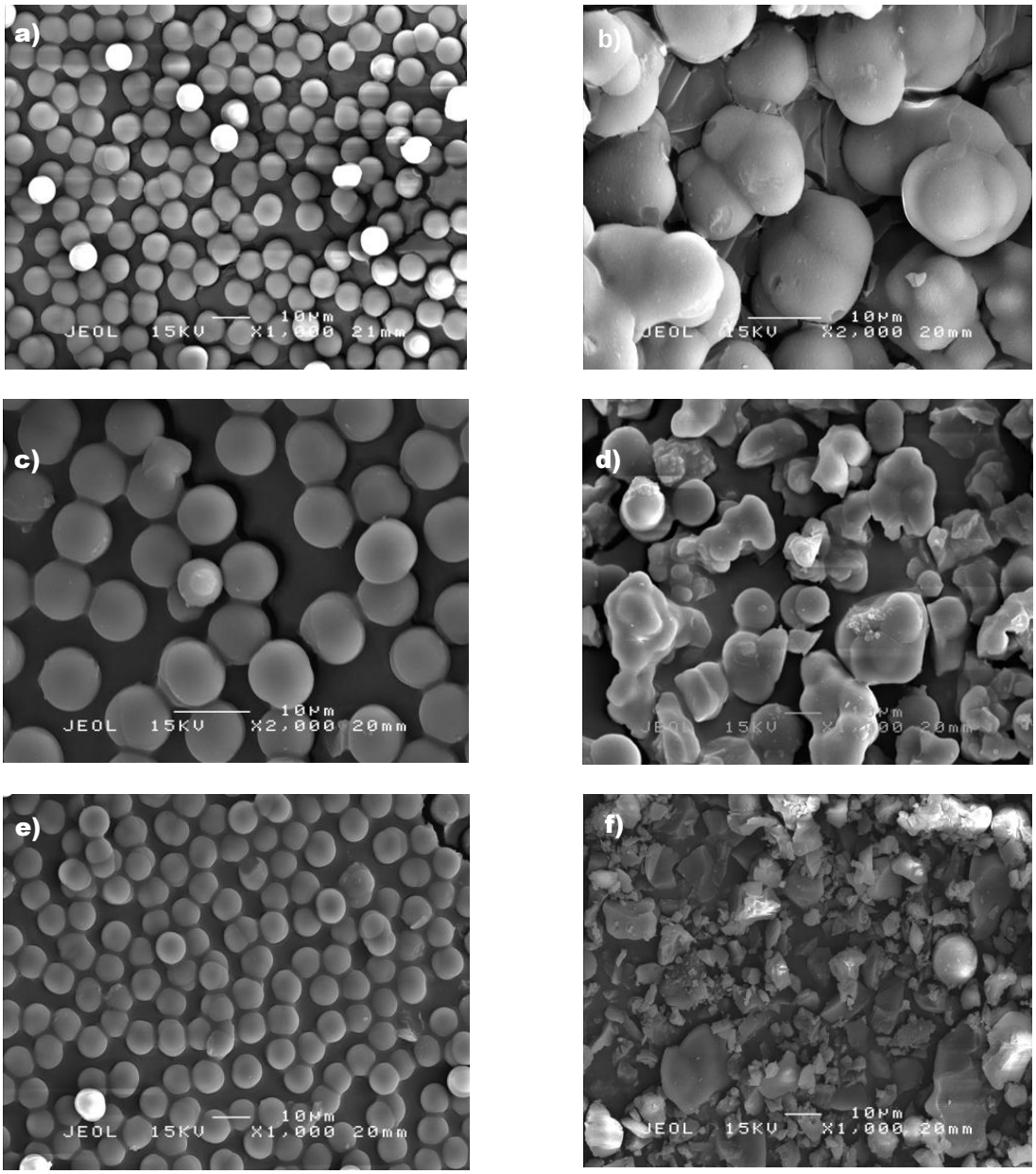


Figure 4. SEM images of: (a) A8, (b) A9, (c) HA8, (d) HA9, (e) MHA8, and (f) MHA9, respectively

Table 4. The particle sizes and dispersities of poly(AN-*co*-DVB-80-*co*-VBC) and HXL poly(AN-*co*-DVB-80-*co*-VBC) before and after chemical modification

Samples	AN/DVB-80/VBC, mol%	Mean particle diameter, μm	Coefficient of variation, %	Dispersity
A8		6.8	4	Monodisperse
HA8	35/60/5	7.2	7	Monodisperse
MHA8		7.4	5	Monodisperse
A9		-	-	Agglomerated
HA9	40/55/5	-	-	Agglomerated
MHA9		-	-	Agglomerated

Table 5. Chlorine content in wt% of poly(AN-*co*-DVB-80-*co*-VBC) before and after hypercrosslinking (HXL) reaction

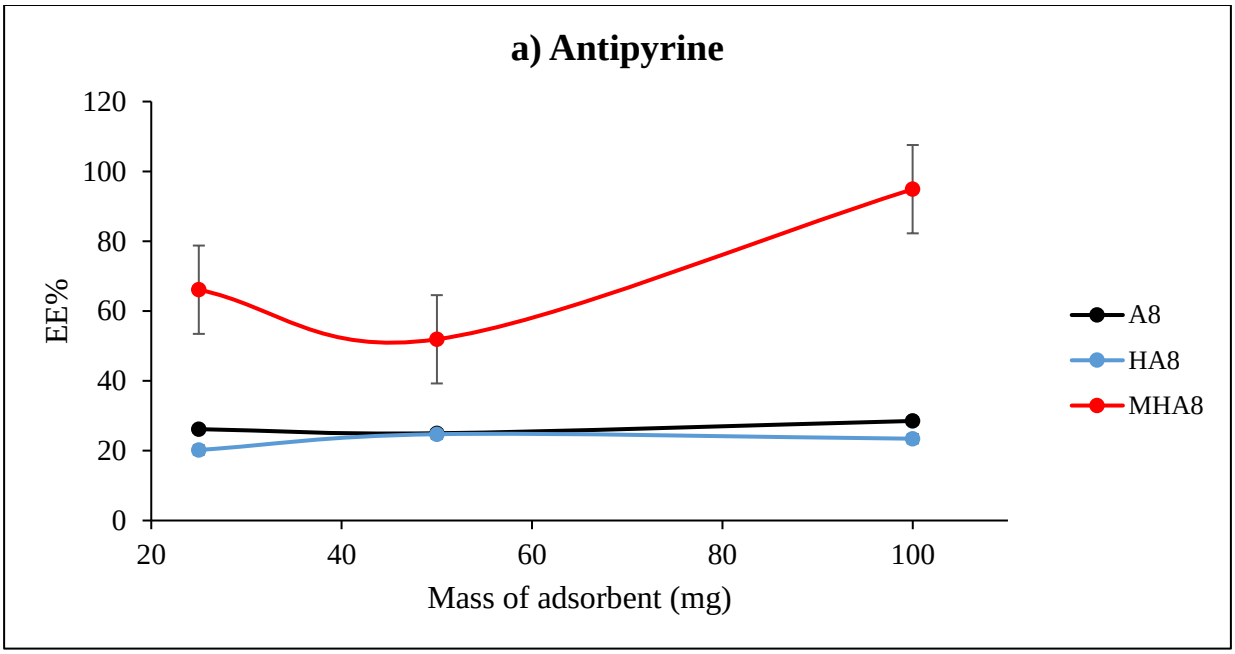
Chlorine content, wt%			
Samples	Before HXL reaction	Samples	After HXL reaction
A8	0.97	HA8	0.61
A9	1.64	HA9	0.92

2. DSPE Extraction Analysis

2.1. Effect of Adsorbent Mass

Different amounts of adsorbent (25, 50 and 100 mg) were used to study the effect of adsorbent mass on the extraction efficiency (EE%) of polar compounds. **Figure 5(a)** shows the influence of adsorbent dosage on the extraction efficiency, EE% of antipyrine. The EE% of MHA8 is the highest compared to those of A8 and HA8 (at all adsorbent dosages). However, the EE% of 25 mg of adsorbent (66%) and EE% of 50 mg adsorbent (52%) showed a difference of 14%. This might be due to the strong binding of the solute on the surface of the 50 mg adsorbent. Strong binding increases resistance to mass transfer during the elution process. This may have resulted in a slight reduction of EE% for 50 mg of adsorbent as compared to that of 25 mg adsorbent. However, the EE% rapidly increased to 95% when 100 mg of adsorbent was used. This observation may be due to the fact that a higher amount of adsorbent reduces the resistance to mass transfer. Meanwhile, the EE% of A8 was comparable to the EE% of HA8. This result shows that the availability of the active surfaces of A8 and HA8 were not dependent on the amount of adsorbent used.

The effects of adsorbent mass on the EE% of pamabrom is shown in **Figure 5(b)**. The EE% of MHA8 is the highest at 53%, with 25 mg of adsorbent mass. The EE% of MHA8 and HA8 significantly increased as the adsorbent mass was increased to 50 mg. This is expected due to more active sites on the surface of MHA8 and HA8 being available for the electrostatic interactions with pamabrom molecules. However, a very small difference of up to 0.1% was observed in the EE% of MHA8 between the results for 50 mg of adsorbent (54.3%) and 100 mg of adsorbent (54.2%). This might be due to the fact that the elution ability of MHA8 was almost the same when 50 mg and 100 mg of adsorbent were used. Hence, the EE% values were similar for both adsorbent dosages. Simultaneously, there was no significant change to the EE% of A8 as the adsorbent mass was increased from 25 to 100 mg. Based on these results, MHA8 was more favorable for the extraction of antipyrine (maximum EE at 95%) compared to that of pamabrom (maximum EE at 54%). The reasons for this observation are discussed in Section 3.2.1.1.



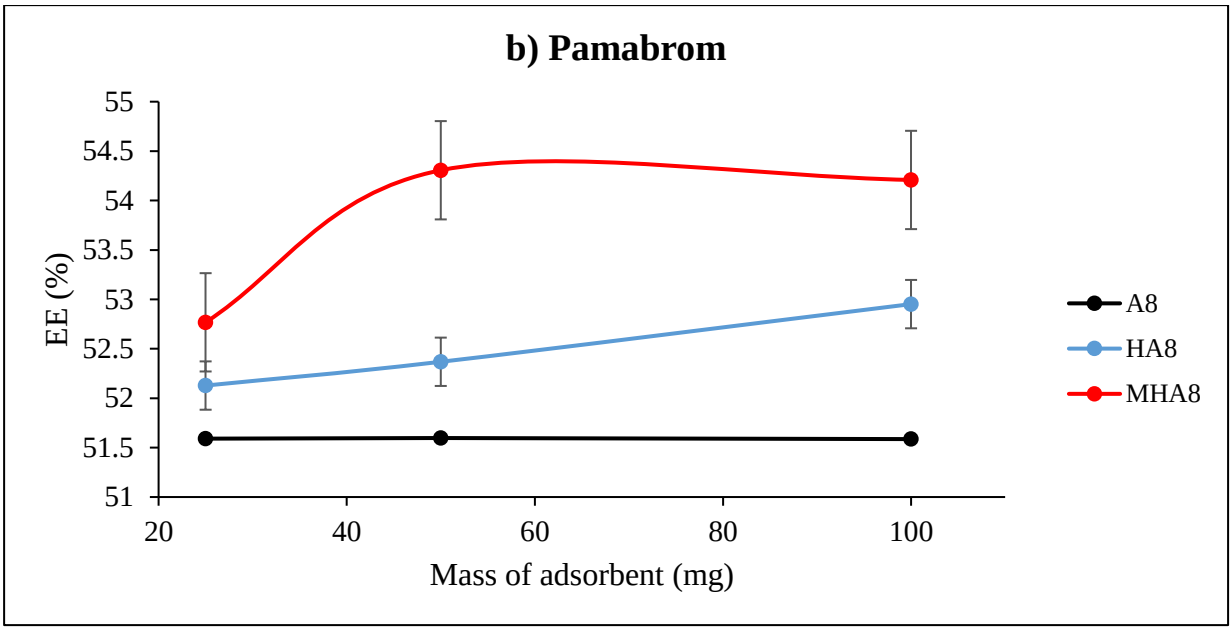


Figure 5. Comparison of extraction efficiency, EE % of A8, HA8 and MHA8, respectively, towards: (a) antipyrine and (b) pamabrom, with different adsorbent mass. **Conditions:** Concentration of antipyrine, 20 ppm; volume of antipyrine solution, 10 mL; extraction time, 8 mins, centrifugation speed, 2000 rpm; elution time, 5 mins; temperature, 25 °C.

2.1.1. Proposed Mechanism of Reaction between Adsorbent and Polar Analytes (Antipyrine & Pamabrom)

The proposed mechanism of reaction between EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) and antipyrine is shown in **Figure 6**. The EDA-HXL-AN/DVB-80/VBC terpolymer demonstrated better extraction performance due to the presence of active sites on the adsorbent surface. The pendant diamine groups (N-H and $–NH_2$) in the EDA-HXL-AN/DVB-80/VBC interact with antipyrine *via* electrostatic interactions. The oxygen atom in antipyrine has a lone pair of electrons that makes it highly electronegative and can form strong electrostatic interactions with hydrogen atoms in the diamine groups of the EDA-HXL terpolymer. The existence of strong π-π non-covalent interactions between antipyrine and EDA-HXL-AN/DVB-80/VBC was also expected due to the presence of aromatic rings in the adsorbent and antipyrine chains.

As shown in **Figure 5(a)** and **5(b)**, the variation in adsorbent dosage indicates that MHA8 has better selectivity towards antipyrine. This might be due to the π-π interactions between antipyrine and the adsorbents that enhance the extraction efficiency up to 100%, as in **Figure 5(a)**. However, this is not the case with pamabrom and the adsorbents, as it resulted in a lower extraction efficiency (~55%, as in **Figure 5(b)**).

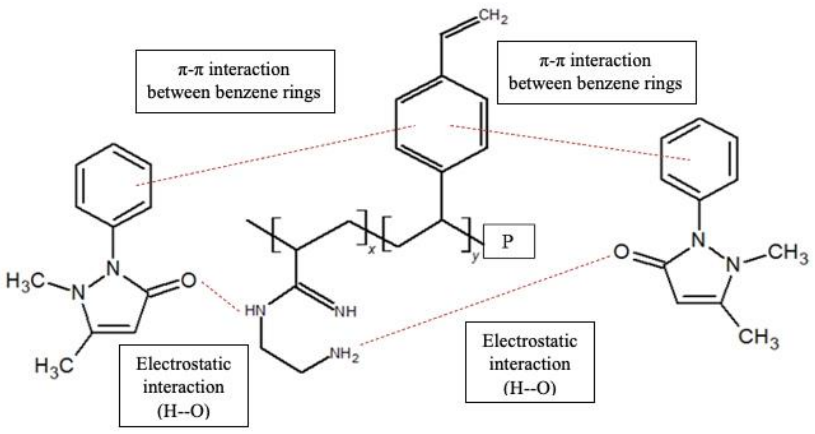


Figure 6. Proposed reaction mechanism of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) (MHA8) and antipyrine.

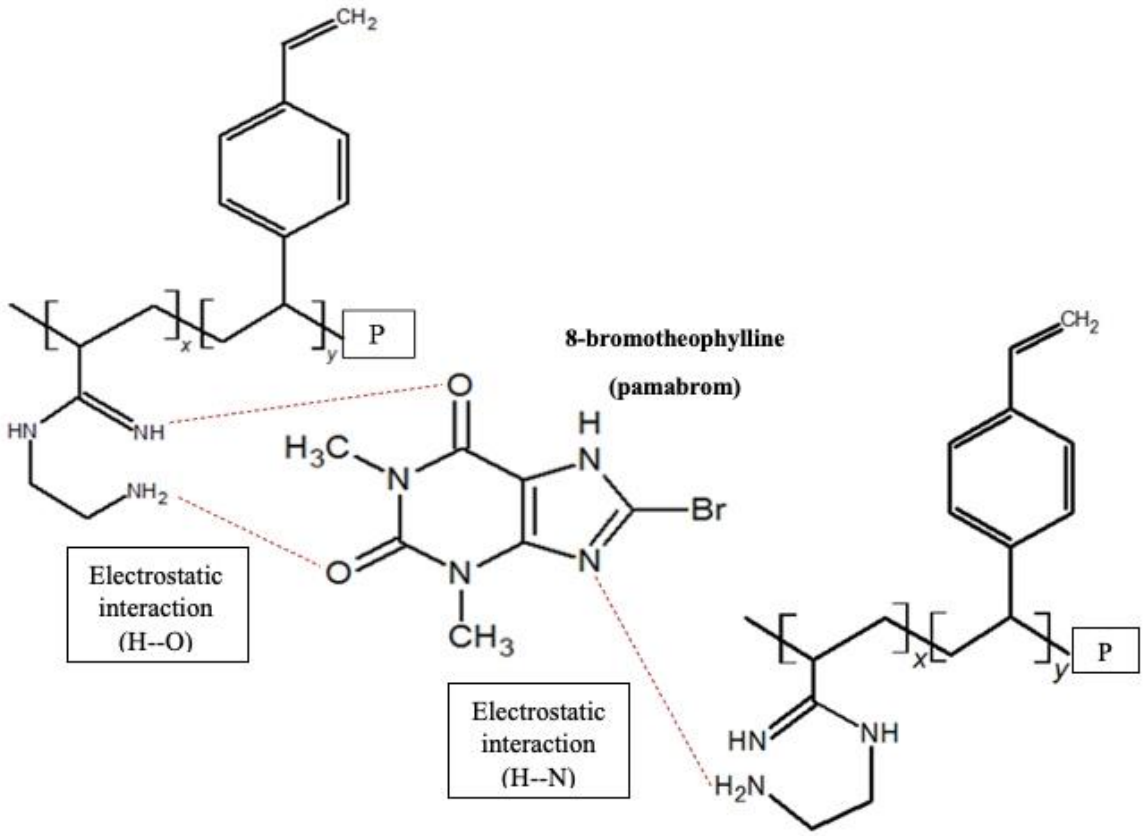


Figure 7. Proposed reaction mechanism of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) (MHA8) and pamabrom.

The polymeric adsorbent (EDA-HXL-AN/DVB-80/VBC) (MHA8), which has a polar diamine group (-NH_2 and N-H), also interacts with pamabrom *via* electrostatic interactions (H-O and H-N). 8-bromotheophylline is the active moiety of pamabrom, which acts as a weak diuretic agent and has been used with some analgesic drugs [30]. The partially positive hydrogen atom in the adsorbent forms electrostatic interactions with lone pairs of electrons from the oxygen and nitrogen atoms of pamabrom. **Figure 7** shows the proposed reaction mechanism of EDA-modified HXL poly(AN-*co*-DVB-80-*co*-VBC) and pamabrom.

2.2. Effect of Extraction Time

Another important factor is the equilibrium extraction time. A centrifugation method was used to facilitate the extraction, so that the extraction phase that contained the target analyte could be easily separated for the elution process. In this study, different extraction times in the range of 10-30 mins were investigated. **Figure 8(a)** shows that the EE% of A8 was comparable with the EE% of HA8. The EE% of MHA8 was the lowest at 10 min (48%) because the active sites on the surface of MHA8 were rapidly filled up with the analytes after 10 min. However, at 10 min, the active surfaces of A8 and HA8 were still highly available for electrostatic interactions with antipyrine molecules. Thus, as the extraction time increased to 20 min, the EE% of A8 was the highest (62%) compared to those of HA8 and MHA8 (54% and 53%, respectively). This was expected due to the slower uptake of antipyrine by A8 compared to the faster uptake of antipyrine by HA8 and MHA8. A similar trend can be seen at 30 min extraction time, where A8 had the highest EE% compared to HA8 and MHA8. These results show that with HA8 and MHA8, an extraction time of less than 10 min produced a faster uptake which then slowed down after 10 min. This can be established from **Figure 5(a)**, in which the EE% of antipyrine using MHA8 was the highest at an extraction time of 8 min, while lower extraction efficiencies were obtained when using HA8 and A8.

Figure 8(b) shows the variation of extraction times for pamabrom. It can be observed that the EE% at 10 min when using A8, HA8 and MHA8 were 98%, 97% and 97%, respectively. Small differences in the EE% for all adsorbents were also observed at 20 and 30 min of extraction time (±1%). This showed that pamabrom was not particularly selective towards HA8 and MHA8, because it had good electrostatic interactions with A8 as well. In addition, the extraction time did not significantly influence the EE% when different types of adsorbents were used.

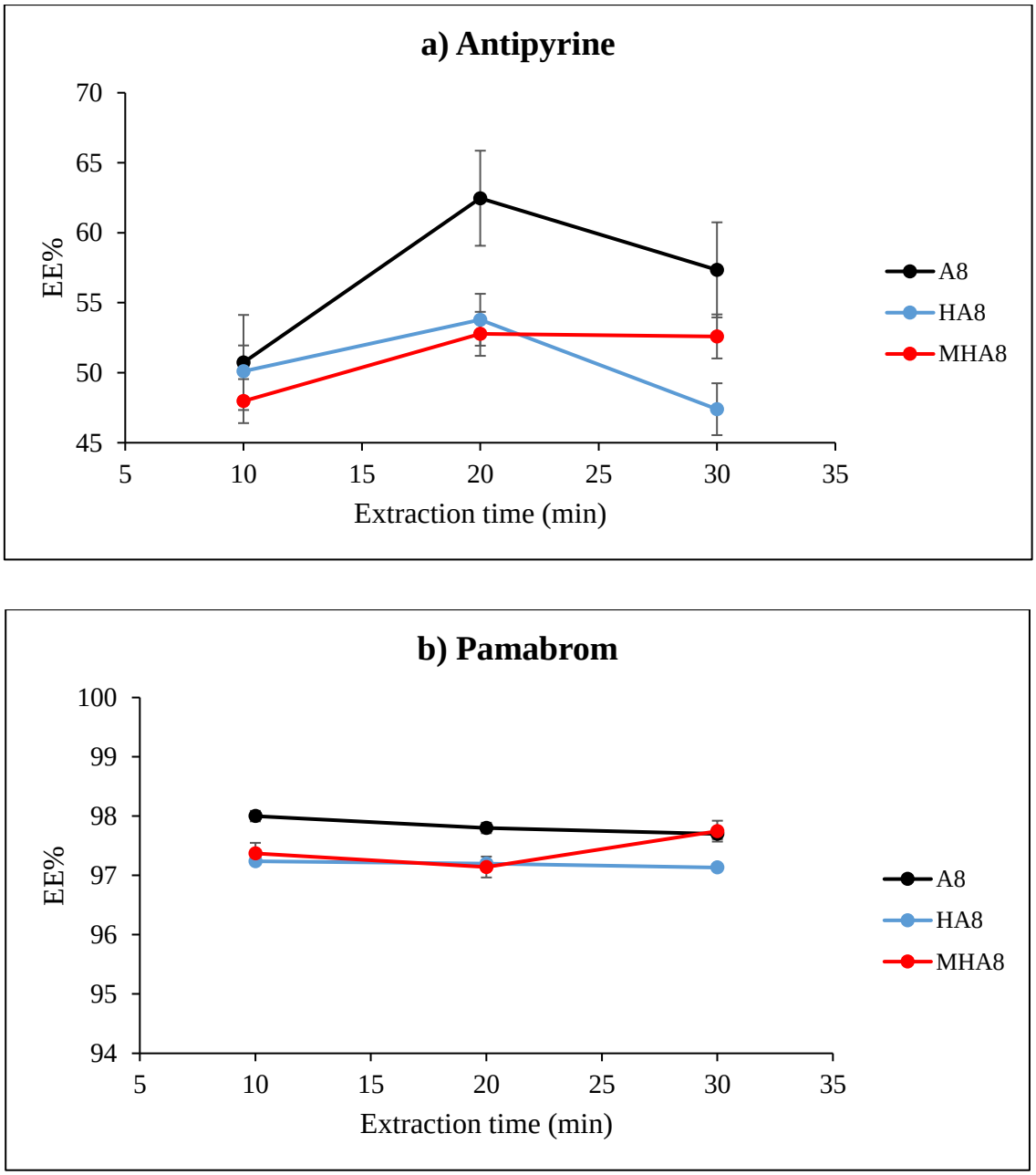


Figure 8. Comparison of extraction efficiency (EE%) of A8, HA8 and MHA8, respectively, towards: (a) antipyrine and (b) pamabrom, at different extraction times. **Conditions:** Concentration of antipyrine, 20 ppm; volume of antipyrine solution, 10 mL; mass of adsorbent, 25 mg; extraction time at 2000 rpm; elution time, 5 mins; temperature, 25 °C.

2.3. Effect of Elution Time

Figure 9(a) shows the influence of elution time on the EE% of antipyrine. In this study, the elution of antipyrine molecules from the surface of adsorbents was carried out using methanol. The EE% of antipyrine from all adsorbents were comparable at 5 min elution time. However, the EE% was the highest for HA8 at 10 min (532%). This observation shows that the desorption of antipyrine was favourable from the surface of the hypercrosslinked polymer at the optimum time (10 min). On the other hand, the desorption of antipyrine from the surface of A8 and MHA8 were almost the same (257 and 284%, respectively) at 10 min elution time. The EE% for all adsorbents were almost the same (~275%) as the elution time increased to 15 min.

Meanwhile, the effect of elution time on the EE% of pamabrom is depicted in **Figure 9(b)**. The EE% of pamabrom from HA8 and MHA8 were comparable at 5 min elution time. The highest EE% was achieved by A8 at 5 min elution time (100%). This can be seen in **Figure 6(b)**, where the EE% of pamabrom from A8 was the highest (at the elution time of 5 min), followed by lower extraction rates with

HA8 and MHA8. However, the EE% was the highest for MHA8 at 10 min (99%). This result shows that the desorption of pamabrom was favourable from the surface of the modified hypercrosslinked polymer at the optimum time of 10 min. On the other hand, the desorption of pamabrom from the surface of both A8 and HA8 were the same (98%) at 10 min elution time. The EE% for all adsorbents were almost the same (~98%) when the elution time increased to 15 min. From these results, it can be concluded that the desorption of antipyrine (from the adsorbents) was more feasible (EE = 200-532%) compared to that of pamabrom (EE = 97-100%). This might be due to the lower selectivity of pamabrom towards the adsorbents compared to antipyrine. Similar observations were made in Section 3.2.1.

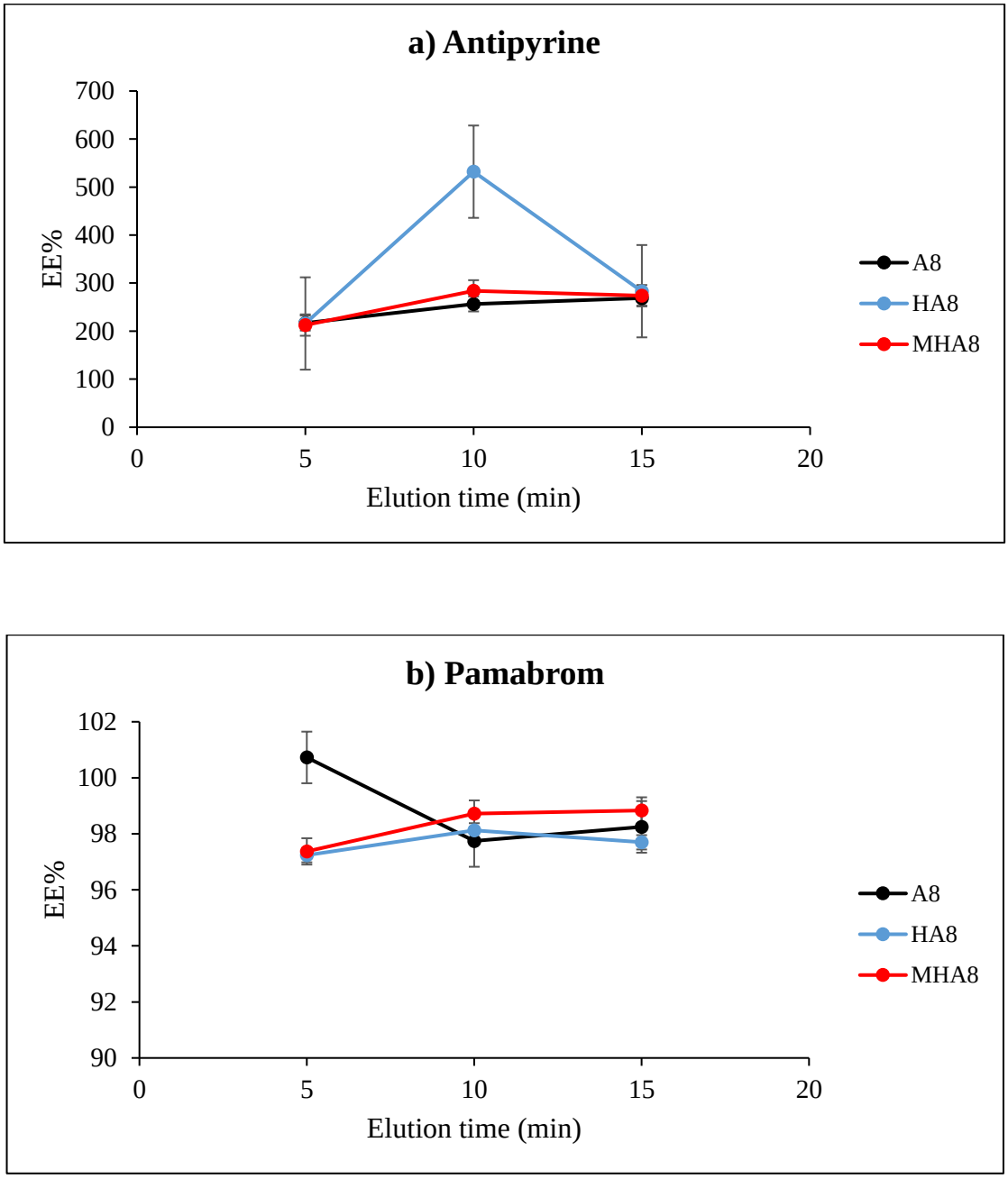


Figure 9. Comparison of extraction efficiencies (EE%) of A8, HA8 and MHA8, respectively, towards: (a) antipyrine and (b) pamabrom, at different elution times. **Conditions:** Concentration of pamabrom, 20 ppm; volume of pamabrom solution, 10 mL; mass of adsorbent, 25 mg; extraction time, 10 mins at 4000 rpm; temperature, 25 °C.

CONCLUSIONS

Poly(AN-*co*-DVB-80-*co*-VBC), hypercrosslinked poly(AN-*co*-DVB-80-*co*-VBC) and EDA-modified hypercrosslinked terpolymers were successfully synthesized in this study as polymeric adsorbents. Our preliminary study on the efficiency of these adsorbents in extracting antipyrine and pamabrom showed that the hypercrosslinked polymer and its modified version was able to extract antipyrine and pamabrom from aqueous solution. It was also shown that the modified hypercrosslinked poly(AN-*co*-DVB-80-*co*-VBC) had a higher extraction efficiency towards antipyrine (up to 100%) than pamabrom (~55%).

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