Electronic Supplementary Material (ESI) for Journal of Materials Chemistry A.

Biodegradable Nano Carbon based Smart Filters for Efficient Remediation of Pharmaceutical Contaminants

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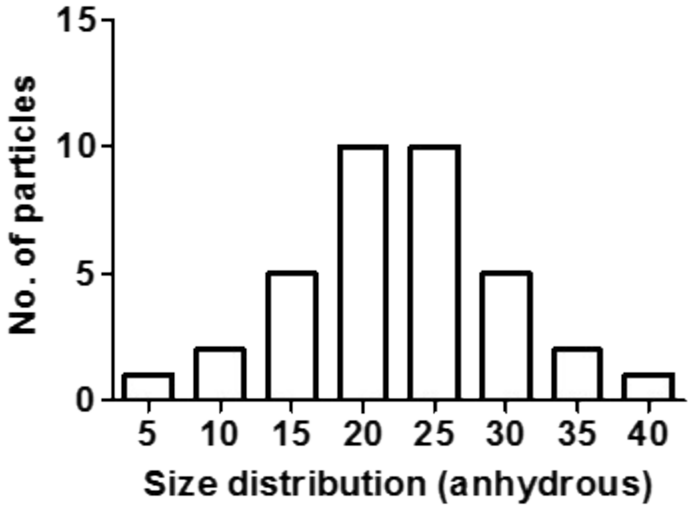


Figure S1. Size distribution of CNP-TCDA particles from TEM.

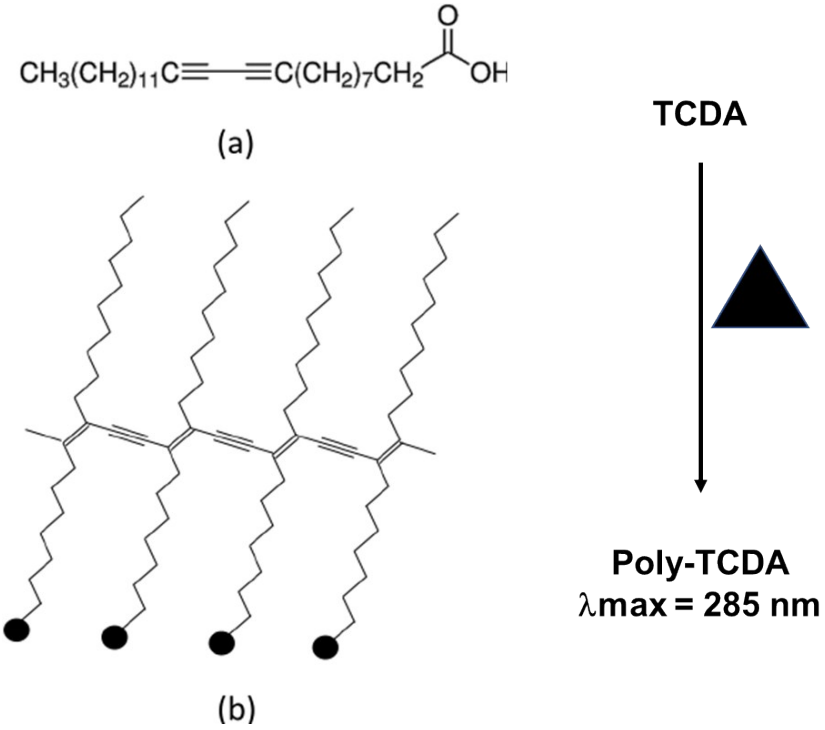


Figure S2. Thermal conversion of (a) TCDA to (b) polyTCDA.

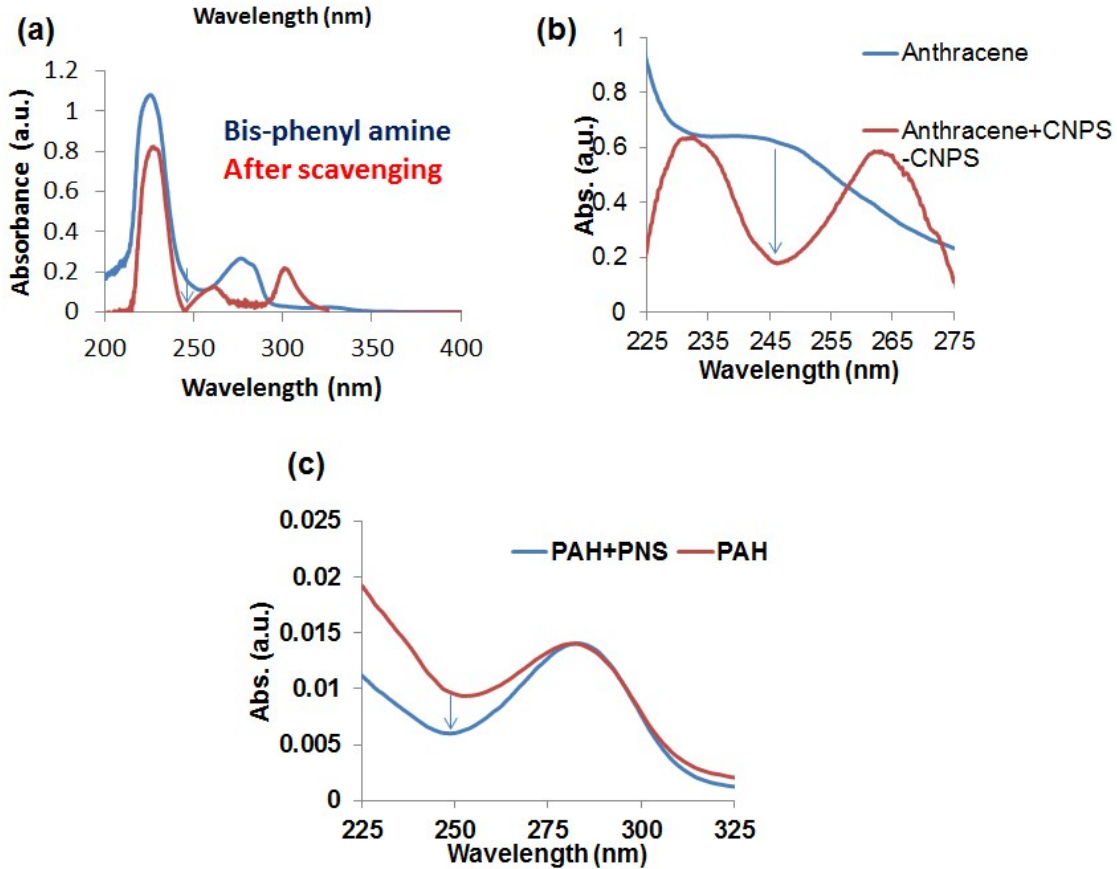


Figure S3. Scavenging of various parent pharmaceutical moieties using PNCS. Scavenging of (a) bis-phenyl amine; (b) anthracene and (c) mixture of polyaromatic hydrocarbons.

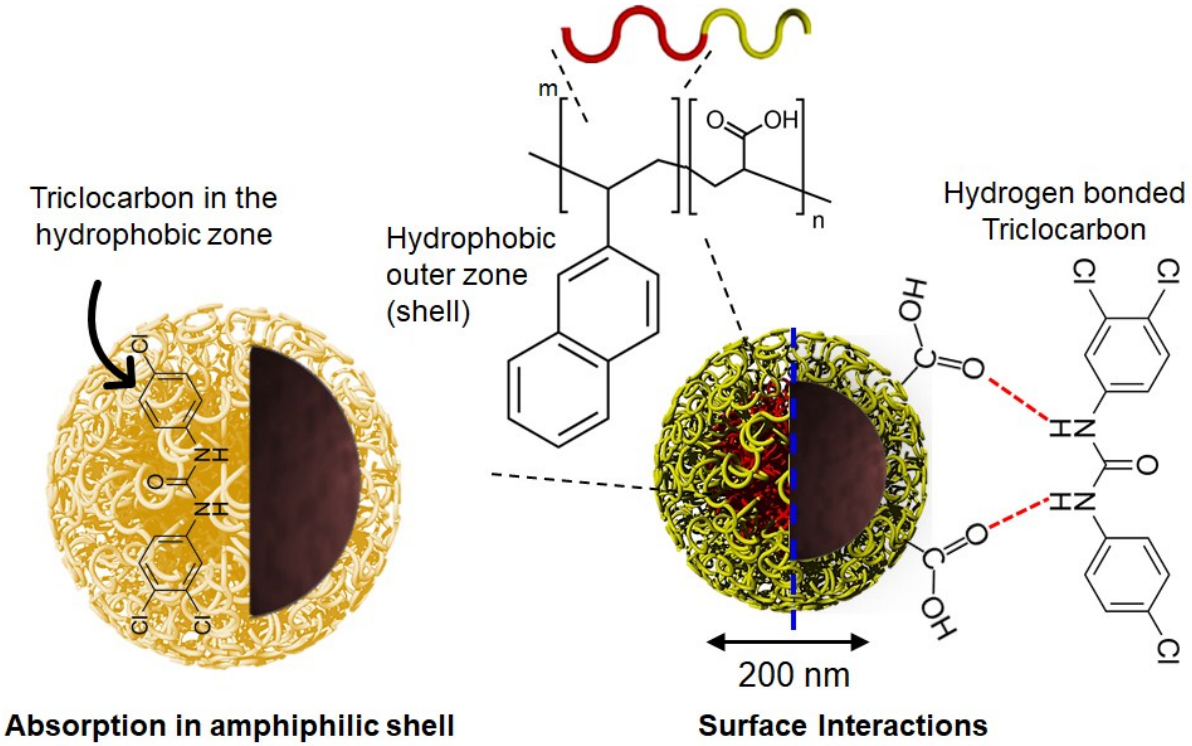
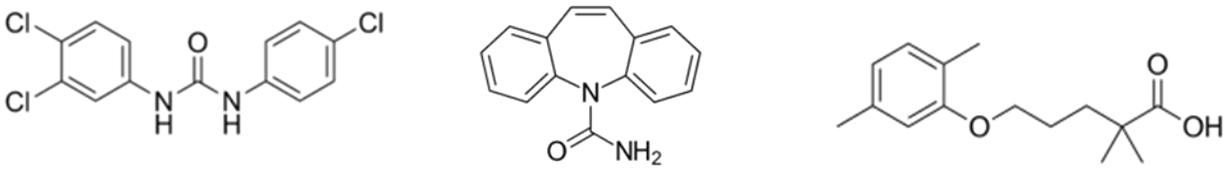


Figure S4. Representational dual mode interaction of PPCP (e.g. triclocarbon 3-(4-Chlorophenyl)-1-(3,4-dichlorophenyl) urea) with PNCS.



Triclocarbon; >99% **Carbamazepine; >99%** **Gemfibrozil; ~65%**

Figure S5. Chemical structure of PPCPs and their scavenging % by PNCS.

Table S1. TOC (%) of PNCS treated samples compared to untreated PPCPs.

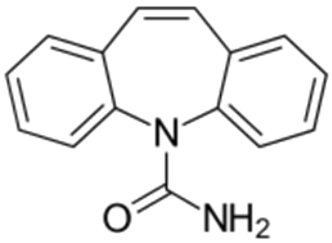
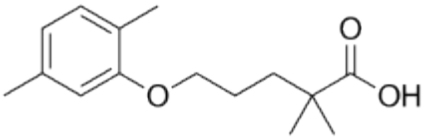
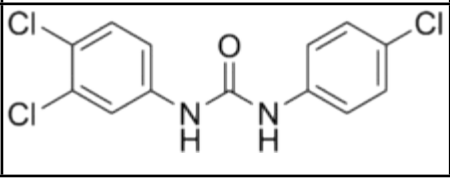
Pharmaceutical compound name	(%) TOC of PNCS treated samples compared to untreated		
	Round 1	Round 2	Round 3
Carbamazepine	23.0±2.3	27±2.7	-13±1.3
Gemfibrozil	13.0±1.3	6±0.6	-8±0.8
Triclocarbon	-9.0±0.9	22±2.2	20±2.0

Table S2. Effect of filtration on % TOC.

Pharmaceutical compound name	(%) TOC of PNCS treated samples compared to untreated		
	Use 1	Reuse 1	Reuse 2
Carbamazepine	1±0.1	19±0.2	14±1.4
Gemfibrozil	4±0.4	13±1.3	8±0.8

Triclocarbon	1±0.1	8±0.8	11±1.1

Table S3. Reuse of PNCS and efficiency of pharmaceutical contaminant removal.

Pharmaceutical compound name	**Pharmaceutical compound chemical structure**	**(%) Removal efficiency after PNCS reuse**		
		Use 1	**Reuse 1**	**Reuse 2**
Carbamazepine		>99	11±1	5±0.5
Gemfibrozil		>65	1±0.1	5±0.5
Triclocarbon		>99	>99	>99

Materials and Methods

PPCP standards carbamazepine, gemfibrozil, and triclocarban were obtained from Restek (Bellefonte, PA, USA). Isotopic standards including D_{10}-carbamazepine, D_6-gemfibrozil, and $^{13}C_6$-triclocarban were purchased from Cambridge Isotope (Andover, MA, USA). Nectar agave (HoneyTree's Organic Agave Nectar, Onsted, MI) was procured from local grocery store, *10, 12*-tricosadiynoic acid from Sigma-Aldrich (St. Louis, MO). Poly(2-vinyl naphthalene-b-acrylic acid) as the diblock copolymer was acquired from Alfa Aesar (Haverhill, MA). Solvents used in the study, including methanol, acetone, and acetonitrile, were purchased from Fisher Scientific (Fair Lawn, NJ, USA). Deionized (DI) water (>18.2 MΩ-cm) was supplied by a Labconco Water Pro Plus system (Kansas City, MO, USA).

Preparation of Pharmaceutical-Nano-Carbo-Scroungers (PNCS) .

The absorption-based remediation of pharmaceutical contaminants requires a multi-component nano-architecture which can create a hydrophobic inner compartment for entrapment. Our strategy

utilizes a biodegradable carbon core hydrophobically modified by a cross linker, 10,12-tricosadiynoic acid (TCDA). It could be produced by thermally cross-linking TCDA onto commercially available agave nectar (an inexpensive sweetener composed of 47-56% of fructose and 19-20% glucose).

The CNP-TCDA core of the PNCS was produced by a hydrothermal method[1-5] of controlled heating in a suspension of 1250 mg/ml of nectar agave (HoneyTree's Organic Agave Nectar, Onsted, MI) and 187.5mg/ml of 10, 12-tricosadiynoic acid (Sigma-Aldrich, St. Louis, MO) in nanopure water in a 20 ml scintillation vial at 250 degrees Celsius for 45 minutes or until all water evaporates and product turns black mass. It was allowed to be soaked in THF overnight then resuspended by sonication (Q700, Qsonica Sonicators, Newtown, CT) in an ice bath (to prevent evaporation) for 24 minutes at one amplitude with intervals of five seconds on and three seconds off. The sonicated suspension was filtered through 0.45μm and 0.22μm PTFE membranes sequentially. Prepared suspensions were characterized for physiochemical characteristics and found to be of Nano dimensions. The suspension was dried out to produce a residue. This residue and Poly (2-vinyl naphthalene-b-acrylic acid) as our diblock copolymer. t a 10:2 mass ratio respectively, was resuspended in THF. The volume of THF used is the minimum required to fully dissolve solutes. The crosslinking was monitored using a UV-VIS Spectroscopy (GENESYS 10 S). To measure the collected samples, a 1 to 20 dilution of the heated sample was prepared in deionized water for each UV-VIS measurement where a stock solution of agave in water at the same concentration was used as a blank. Water was then added rapidly to THF suspension of particle mass at a twice the volume of THF to produce the block polymer coated nanoparticles known as the pharmaceutical Nanocarboscavenger (PNCS). This suspension was placed in a vacuum to dry and then scraped and ground into powder form.

Physico-chemical Characterizations

Dynamic Light Scattering

The hydrodynamic size distribution of the CNP-TCDA was determined through dynamic light scattering measurements on a Malvern Zetasizer ZS90 instrument (Malvern Instruments Ltd, United Kingdom) at fixed angle of 90^{o}. A 10 μL of particle suspension was mixed with 990 μL of THF to run the samples in DLS machine. A photomultiplier aperture of 400 nm was used, and the incident laser power was so adjusted to obtain a photon counting rate between 200 and 300 kcps. Measurements for which the measured and calculated baselines of the intensity autocorrelation function were within 0.1% range were used for diameter values. All measurements were carried out in triplet of thirteen consecutive measurements. Similarly, hydrodynamic diameter of PNCS was determined in water medium.

UV-Vis Spectroscopic Study

The absorbance of the PNCS suspensions (0.1 mg/mL) and aromatic hydrocarbons dissolved in water were recorded in spectrum range of 200 to 800 nm on a GENESYS 10 UV−Vis spectrophotometer (Thermo Scientific).

Transmission Electron Microscopy (TEM)

Anhydrous state morphology and size of PNCS were acquired by transmission electron microscopy. A 5 μL volume of 0.1 mg/mL PNCS was coated on copper grid and air dried before being dried under vacuum for 4h. TEM was acquired on JEOL 2100 Cryo TEM at MRL, UIUC facility.

PCCP Scavenging Procedure

Briefly, three PPCP stock solutions (Carbamazepine, gemfibrozil and triclocarban) were added to deionized water and mixed thoroughly, yielding initial concentration of 0.2 µg/L. Five milliliters of each samples were taken in 20 ml scintillation vial and 10 mgs of PNCS added to it. Magnetic stir bars were put in the scintillation vial and stirred for 24hrs. This treatment was repeated three times. The treated samples centrifuged at 11,000 rpm for 10 minutes and then filtered through a 0.45-μm membrane (Iso-Disc, Supelco, Bellefonte, PA) using a syringe. All samples were stored at 4^{o}C and analyzed within a week using liquid chromatography tandem-mass spectrometry (LC-MS/MS). Preliminary experiments showed that targeted PPCP concentrations were stable at this temperature and time period.

LC-MS/MS Analysis

Concentrations of PPCPs were determined by LC-MS/MS (Waters, Quattro Macro, QA1140, Milford, MA) based on our previously developed methods (Li et al., 2013). Isotopic standard (100 ng for each chemical) was spiked into the sample extract and 30 µL of sample was injected for analysis. Three PPCPs investigated in this work were separated on a symmetry C_{18} column (3.5 µm particle size, 2.1×150 mm, Waters) by a high-performance liquid chromatography (HPLC) system (2695 module, Waters). A gradient separation was achieved using two mobile phases: solvent A, water containing 0.1% ammonium acetate and 0.1% acetic acid; and solvent B, 1:1 methanol: acetonitrile. The gradient started with 90% solvent A and 10% solvent B and was maintained for 2 minutes. Then the gradient was ramped up to 5% solvent A and 95% solvent B linearly in 13 minutes and maintained for 8 minutes. The gradient was changed back to 90% solvent A and 10% solvent B after 0.5 minutes and re-equilibrated for 5.5 minutes. The flow rate was 0.19 mL/min.

The HPLC system was coupled with a Quattro Macro mass spectrometer (QA1140, Waters, Milford, MA) equipped with an electrospray ionization (ESI) source. For the measurement of three targeted PPCPs, the mass spectrometer was operated in positive and negative ESI mode simultaneously with optimized instrument conditions: desolvation gas flow rate 650 L/min; capillary voltage 3.0 kV for positive and 3.5 kV for negative mode. Quantitative analysis was performed in the multiple reaction monitoring (MRM) mode. Optimized collision energy, cone voltage, and retention times for each PPCP are listed in Table 1.

Effect of PNCS scavenging on total organic content (TOC) of contaminated solution

Experiment was performed by using scavenging experiments including triple scavenging with new batch of PNCS (1 mg/mL) each time. Triclocarbon (50 µg/L), Carbamazepine (223 µg/L) and Gemfibrozil (202 µg/L) were used as PPCP contaminants. Filtered solutions were investigated on instrument: TOC-VCPN of ISTC, UIUC, IL for TOC calculation.

Surface area calculation

Surface area of PNCS was calculated by the formulae used by Nath and Barbhuiya (2014).[6]

The formulae used was:

$S = 6000/(d*\rho)$

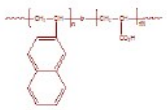
where S = surface area; d = diameter and ρ = density.

Reuse of PNCS

Experiment was performed by reusing PNCS (1 mg/mL) for three batches of contaminated waters with Triclocarbon (50 μg/L), Carbamazepine (223 μg/L) and Gemfibrozil (202 μg/L). Filtered solutions were investigated by LC/MS/MS to calculate the % removal efficiency after reuse."

Characterization details of 2VN-b-AA is 30.8-b-24.0 copolymer:

Sample Name:
Poly(2-vinyl naphthalene-b-acrylic acid)



Sample # P3311C-2VNAA

Composition:

Mn x 10^3 2VN-b-AA	PDI
30.8-b-24.0	1.09

Synthesis Procedure:
The details are given in the following paper:

Faquan Zeng, Mu Yang, Jianxin Zhang, Sunil K. Varshney. ***Synthesis and characterization of block copolymers from 2-vinylnaphthalene by anionic polymerization***, Journal of Polymer Science Part A: Polymer Chemistry, 40, 24, 4387-4397 2002.

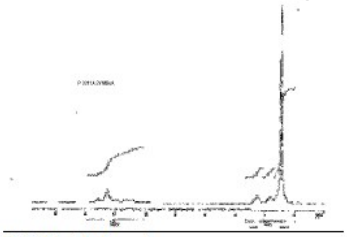
Characterization:

An aliquot of the anionic poly 2-vinyl naphthalene block was terminated before addition of D3 and analyzed by size exclusion chromatography (SEC) to obtain the molecular weight and polydispersity index (PDI). The final block copolymer composition was calculated from ^{1}H-NMR spectroscopy.

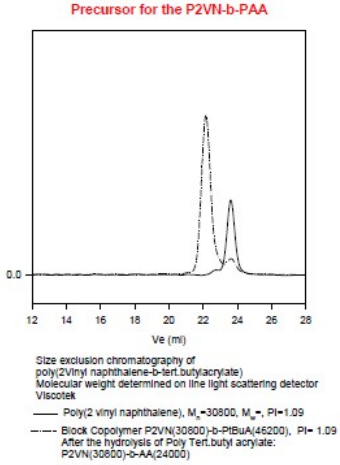
Solubility:

Poly(2-vinyl naphthalene-b-AA) block copolymer is soluble in THF , Dioxane.

^{1}H-NMR Spectrum of the block copolymer:



SEC of the block copolymer :



Size exclusion chromatography of
poly(2Vinyl naphthalene-b-tert.butylacrylate)
Molecular weight determined on line light scattering detector Viscotek

—— Poly(2 vinyl naphthalene), M_w=30800, M_w=, PI=1.09

-·-·- Block Copolymer P2VN(30800)-b-PtBuA(46200), PI= 1.09
After the hydrolysis of Poly Tert.butyl acrylate:
P2VN(30800)-b-AA(24000)

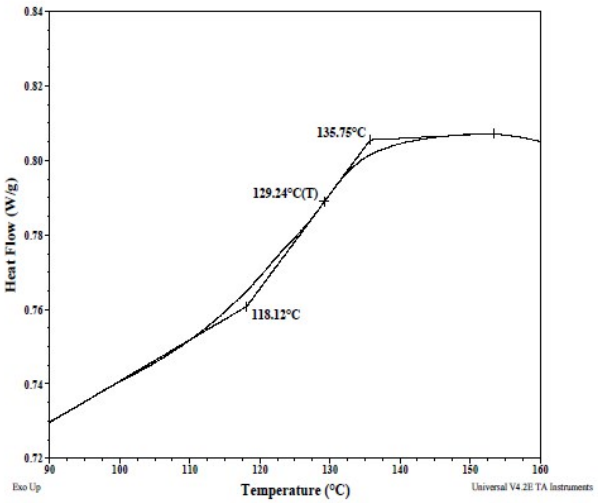
Thermal analysis of sample P3311A-2VNtBuA used to convert 2VNAA

Thermal analysis of the samples was carried out on a TA Q100 differential scanning calorimeter at a heating rate of 10°C/min.The midpoint of the slope change of the heat flow plot of the second heating scan was considered as the glass transition temperature (T_g).

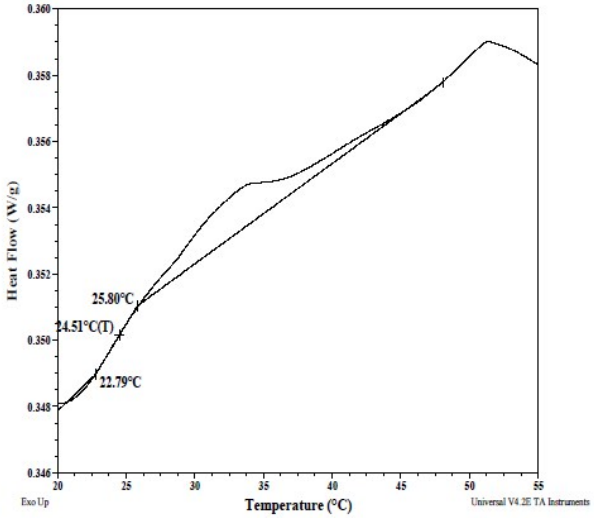
Glass transition temperature at a glance

T_g for PS block	129∘C
T_g for nBuMA block	24∘C

Thermogram of P2VN block:



Thermogram for tBuA block



Reference.

1 S. K. Misra, I. Srivastava, I. Tripathi, E. Daza, F. Ostadhossein, and D. Pan, *J. Am. Chem. Soc.* 2017, **139**, 1746.

2 S. K. Misra, F. Ostadhossein, E. Daza, E. V. Johnson and D. Pan, *Adv. Func. Mat.* 2016, **26**, 8031.

3 S. K. Misra, P. Mukherjee, H. H. Chang, S. Tiwari, M. Gryka, R. Bhargava and D. Pan, *Sci. Rep.* 2016, **6**, 29299.

4 S. K. Misra, H. H. Chang, P. Mukherjee, S. Tiwari, A. Ohoka, and D. Pan, *Sci. Rep.* 2015, **5**, 14986.

5 I. Srivastava, S. K. Misra, I. Tripathi, A. Schawrtz-Duval and D. Pan, *Adv. Biosystems* 2018, DOI: 10.1002/adbi.201800009.

6 B. Nath and T. F. Barbhuiya, J. Chem. Pharm. Res., 2014, 6, 608-610.