PREPARATION AND CHARACTERIZATION OF MOLECULARLY IMPRINTED O-CRESOL VIA SOL-GEL POLYMERIZATION

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Abstract- In this study, a new composite of o-cresol molecularly imprinted polymer was prepared via sol-gel polymerization using o-cresol as the template molecule, 3-propyl(metacrylate)trimethoxysilane (3-PMTMOS) as the functional monomer, tetraethoxysilane (TEOS) as the cross-linker and ethanol as the porogenic solvent. This analyte was selected as a template due to the fact that it is one of toluene metabolites. The molecularly imprinted polymer (MIP) was employed as an adsorbent for the extraction of o-cresol, a metabolite in urine sample for the monitoring of occupational toluene exposure in workers. The MIP prepared using 800 µL of 3-(propylmethacrylate)trimethoxysilane), 12 mL of ethanol, 12 mL of TEOS,0.05 mmol o-cresol and 400 µL of Hydrochloric acid was found to exhibit better sorption for o-cresol. The characterization of MIP and NIP were observed using Fourier transform infra-red (FTIR), while texture properties by N2 adsorption analysis and Field emission scanning electron microscopy- energy dispersive x-ray (FESEM-EDX).

Keywords- o-cresol, Toluene metabolite, Molecularly imprinted polymer, Sol-gel polymerization.

I. INTRODUCTION

Nowadays, analysis of biological sample is very challenging and tedious [1]. It is due to the biological samples such as plasma and urine samples can affect the adsorbent physical properties and the adsorbent can be deteriorated after handling of few samples. Moreover, the destruction of adsorbent during extraction using micro-extraction packed sorbent technique is became serious problems. Therefore, preparing stable, durable and reusable adsorbents is an important challenge today [2], [3].

One of famous technique for enhance the analyte for sample preparation and selective clean-up is molecularly imprinted polymer[4], [5]. Imprinting technique is based on the prearrangement of template-functional monomer complex in a facilitating solvent and it will produce specific recognition site for binding with analyte [6].

In this present study, we introduce a novel and robust adsorbent synthesis and prepare by sol-gel polymerization. Sol-gel polymerization utilizes mild acid catalysed conditions to achieve hydrolysis and conditions using a numerous silane monomer. Gelation of the silane such as 3-(propylmethacrylate) trimethoxysilane under aqueous condition with ethanol in the presence of the template molecule leads to the imprinted sol-gel. Small pores (2-50 nm) and high surface area (> 200 m^2/g) was produced when sol-gel polymerization synthesis by acid catalyzed [7]. This technique have significant potential in development of thin film and layers [8]. Most researcher were found that the sol-gels adsorb a lower total uptake and significantly lower non-specific binding [9], [10].

Toluene has been the most widely used organic solvent in the industries in this decade [11]. It has been reported that exposure to high concentration of toluene will lead to a series of diseases such as acute and chronic respiratory effects, functional alterations of the central nervous system, mucosa and dermal irritations and chromosome aberrations [12]–[14]. Inoue et al., (2007) defined the biomarker of toluene exposure excreted in urine are 82.3% hippuric acid, 0.06% o-cresol and 0.03% benzylmercapturic acid [15]–[17]. However, for hippuric acid metabolites it not only reflects toluene exposure, but also by the intake of food and drink containing benzoic acid. Therefore, it is difficult to determine positive results are specifically due to toluene exposure, especially is low exposure to toluene [18]. O-cresol has been suggested used as a biomarker, especially in the determination of low level of exposure to toluene [14], [19]. Because of that reason, this study was strictly concentrated on o-cresol metabolites. In this study, o-cresol was used as template, 3-(propylmethacrylate)trimethoxysilane as a monomer, tetraethoxy silane (TEOS) as cross linker and acetic acid as catalyst. Moreover, the adsorption capacity and imprinting factor using this molecularly imprinted polymer (MIP) was determined by gas chromatography-flame ionization detector (GC-FID). The kinetic adsorption and static adsorption of developed MIP was evaluated and its physical properties were characterized by FESEM, N_2 adsorption, and FTIR. The developed MIP offered an alternative method of clean up and determination of o-cresol, carrying the benefit of simplicity, low cost and sufficient sensitivity, without any large volumes of organic solvent and robust.

II. EXPERIMENTAL

2.1. Materials

Tetraethoxylsilane (99% TEOS) and 3-propyl(methacrylate)trimethoxysilane (99% 3-

PMTMOS) were purchased from Sigma-Aldrich, USA and used as a receive, o-cresol 99.9% ($C_7 H_8 O$, MW 108.14 g/mol), hydrochloric acid (HCl) 37%, acetic acid (Analytical grade), ethanol (AR) were purchased from Merck Darmastand, Germany.

2.2. Preparation of sol gels

All of the sol gels contained TEOS and different amount of 3-PMTMOS. The preparation consisted of two stages: firstly the hydrolysis without o-cresol and next step condensation in the presence of o-cresol. A 12 mL of ethanol was mixed with 12 mL of TEOS. A 800 µL quantity of 3-PMTMOS was then added. Following this 400 µL of concentrated HCl followed by 4 mL of distill water were then added and the mixture left stirring for 2 hour at room temperature. After that, 108.14 mg of o-cresol dissolve with minimum of ethanol and mark up with water to 20 mL. The solution was added to 16 mL of the imprinting mixture and stirred for 10 minute. A non-imprinted sol-gel was prepared under the same conditions, but with the omission of o-cresol. Condensation was allowed to progress at 80°C for 16 hour and then for 1 week at room temperature. Following this the sol-gel was crushed with a mortar and pestle and sieved [17]. The crushed sol-gel were then washed to remove the template by soxhleet extraction in methanol: acetic acid (9:1) by volume for 24 hour [20].

2.2. Fourier Transform Infra-Red (FTIR), Brunauer-Emmett-Teller (BET) and Field Emission Scanning Electron Microscopy- Energy Dispersive X-ray (FESEM-EDX)

FTIR spectrometry was used to identify the functional groups in materials. Sample disks were made by mixing 1 mg of MIP o-cresol, NIP and MIP o-cresol unleached with 150 mg of KBr, respectively. Data spectrum was analyzed in the 400 to 4000 cm^{-1} region.

Nitrogen adsorption-desorption experiments were carried out on Micromeritics Triflex with a bath temperature 77K. Surface areas were determined using the Brunauer-Emmett-Teller (BET) theory, and pore size distributions were calculated using Barrett-Joyner-Halenda (BJH) theory.

The physical and characterization of MIP o-cresol, NIP and MIP o-cresol unleashed were analyzed using Field Emission Scanning Electron Microscope (FESEM) and elemental analysis of elemental diffraction x-ray (EDX). Firstly, C tape was adhered on sample stage. Then MIP o-cresol, NIP o-cresol and MIP o-cresol unleached were spread on C tape ad loose powder were blown off. Finally, the samples were air dried and sputter-coated with 4 nm of gold particles before using.

2.3 Binding experiment

2.3.1 Optimization of solid to liquid ratio

10 mg, 20 mg, 30 mg, 40 mg and 50 mg MIP o-cresol and NIP were added into 10 mL 2 mg/L o-cresol standard and the mixtures were shaken for 45 minute at room temperature. Then the mixtures were separated through centrifugation and the amount o-cresol in the supernatant was analyzed by GC-FID.

2.3.2 Optimum pH environment

To determine the adsorption capacity, 30 mg of MIP o-cresol and NIP sorbent was added into 10 mL 2 mg/L o-cresol standard. The pH values of the environment were carried out at a range of 4.0 to 9.0 with HCl (0.1 mol/L) or NaOH (0.1 mol/L). After shaking for 45 minute (optimum time) to ensure adsorption equilibrium, the mixtures were separated through centrifugation and the o-cresol concentrations in the supernatant were measured by GC-FID.

2.3.3 Static adsorption experiments

To determine adsorption capacity, 30 mg of MIP and NIP sorbent was added into 10 mL o-cresol standard with varying initial concentrations (0.6-10 mg/L). The resultant mixture was shaken for 45 minute under room conditions, and then separated by centrifuge and the o-cresol in the supernatant was measured by GC-FID. The equilibrium adsorption capacity (Q mg/g) of the MIP or NIP for o-cresol was calculated as following Eq. (1):

$$Qe = (Co - Ce)V/M$$

where Co and Ce were the initial and final concentrations (mg/L) of o-cresol in the tested solution, respectively, V (mL) was the solution volume and M (mg) was the weight of the sorbent.

The specific recognition property of MIP is evaluated by imprinting factor (γ), which is defined as:

$$\gamma = Q_{MIP} / Q_{NIP}$$

where Q_{MIP} and Q_{NIP} were the amount of the template absorbed on MIP and NIP, respectively.

2.3.4 Kinetic adsorption experiment

30 mg of MIP and NIP was placed in a centrifuge tube and mixed with 10 mL of 2 mg/L o-cresol standard (pH=6.0), respectively. The resultant mixture was shaken at room temperature for an interval of time and then centrifuged. The concentration of o-cresol in the supernatant was measured by GC-FID.

III. RESULTS AND DISCUSSION

3.1. Preparation of MIP Cresol

The synthesis diagram of MIP cresol preparation was shown in Fig 1. In this procedure, 3-PMTMOS was used as the functional monomer and interacted with

cresol mainly through the hydrogen and van der waals interactions [21]–[23]. TEOS acting as a cross-linker reagent was easy to hydrolyze under the existence of acetic acid catalyst. In general, these hydrolytic products rebound the template in the imprinting network in the polymer material.

In this situation, the cresol-imprinted sites were obtained by the hydrogen bond coactions generated between the CH_2 from 3-PMTMOS and hydroxyl group of cresol. Furthermore, C=O from 3-PMTMOS and CH_3 group from cresol was generated the van der waals interaction. A large number of cresol special cavities were formed in the polymer material after removing the binding cresol. These imprinted cavities were complementary to the cresol molecules in size and chemical property.

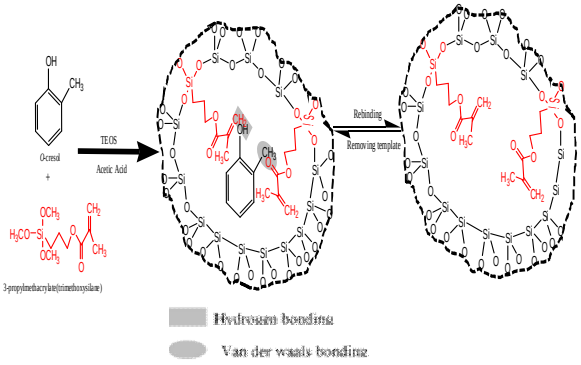


Fig. 1. Scheme for the synthesis of MIP

It is well known that molecular recognition capability of MIP is affected by many factors such as porogen, the amount of monomer and the amount of cross-linker [24]. However, this studied evaluated the amount of monomer only for specific recognition ability of MIP for o-cresol molecules tabulated in Table 1, and it was found that the prepared MIP by using 800 µL had greater adsorption capacity (0.99 mgg^{-1}) and better imprint factor(IF) ϒ (4.95).

Table 1. The adsorption capacities and the imprint factor of the prepared polymer using different amount of monomers (ethanol (12 mL) as the reaction solvent and TEOS (12 mL) as the cross-linker).

No	3-PMTMOS (µL)	HCl (µL)	Q (mgg^{-1})	Imprint factor (IF)
MIP 1	600	400	0.82	4.31
NIP 1	600	400	0.19	
MIP 2	700	400	0.92	4.38
NIP 2	700	400	0.21	
MIP 3	800	400	0.99	4.95
NIP 3	800	400	0.20	
MIP 4	900	400	0.95	4.31
NIP 4	900	400	0.22	

3.2. Characterization of MIP cresol. NIP Cresol and MIP cresol unleached

3.2.1 FTIR

They are three spectrums were analyzed by IR spectroscopy, which is demonstrated the non-imprinted polymer, MIP unleached and MIP leached. Fig. 2 shows the most distinctive infrared absorption bands related to the generation of sol gel. In the 3400-3200 cm^{-1} region, the stretching due to residual water and hence it was observed at 1638 cm^{-1} too [7], [25]. In addition, the observed featured around 1072-1074 $cm^{-1}$and 950-958 cm^{-1} indicate the Si-O-Si and Si-OH is stretching vibration. Furthermore, the peak at 2960 cm^{-1} in Fig. 1 (b) was produced by the stretching vibration of CH_3 and the bands at 1694 cm^{-1} was attributed to the phenyl vibration, however, these peaks could not be found it other figures such as Fig. 1 (a) and 1 (c) [23]. FTIR spectrum of NIP and MIP leached was similar, this spectrum demonstrating that template molecules (cresol) were successfully removed from this materials.

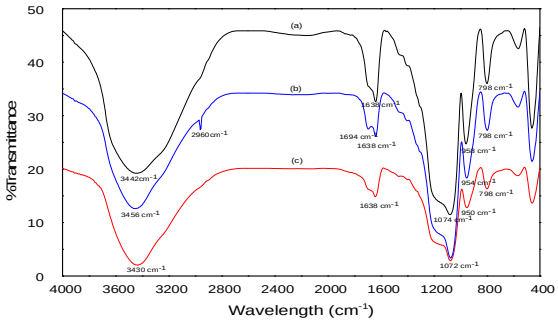


Fig.2. FTIR absorption spectra for (a) NIP (b) MIP Unleached and (c) MIP Leached.

3.2.2 BET Analysis

The BET data show that surface area, pore volume, external diameter and pore diameter of MIP leached, MIP unleached and NIP were tabulated in table 2. The surface area, external diameter and pore volume of MIPs were slightly higher compare to NIP. This was caused by the presence of the cavity recognition sites of the template in the MIPs polymer matrix. Hence, it is confirm that the possibility of higher binding capacity of the MIPs than NIP. Spivak (2005) described that the typical value for the surface area of the imprinted polymer are in the range 100-400 m^2/g, in this case both of MIP leached, MIP unleached and NIP under this BET value. However, for average pore diameter of MIPs and NIP in mesoporous form is in the range 2-100 nm in diameter [26]–[28]. Pore volume, surface area and external surface area of MIP leached increase than the MIP unleached. It is due to the molecule template was removed from the material and create more recognition cavity, hence this is increasing the volume of pore and surface area inside the polymer material.

Table 2. Surface area and pore analysis of NIP, MIP unleached and MIP Leached by nitrogen adsorption.

Polymer	BET surface area, S_{BET} $(m^2/g)^a$	External Surface area, S_t $(m^2/g)^b$	Pore volume $(cm3/g)^c$	Pore Diameter $(Å)^d$
NIP	224.3	115.9	0.1422	18.06
MIP unleached	318.4	133.7	0.1750	14.87
MIP leached	547.9	422.1	0.5314	22.02

[a]Surface area from multipoint BET value on a eleven-point linear plot, [b]External surface area obtained from t-plot, [c]BJH method cumulative desorption pore volume, [d]BJH method desorption pore diameter

3.2.3 FESEM Analysis

The microscopic morphological structures of NIP, MIP unleached and MIP leached were identified using FESEM under 100,000x magnification. As shown in Fig. 3, significant differences between MIP and NIP can be observed from the morphological images. Fig. 2 (a) and (b) illustrates the rough and scraggy images and porous morphology, while for fig. 2(c) demonstrates smooth and slippy images and semi-porous morphology [29]. In addition, the scraggy and rough images is due to the cladding and filling action of the crosslinking polymer layer [30]. However, for MIP leached and MIP unleached no significant differences in morphological structures only the agglomerate shape is slightly higher in MIP unleached morphological images. It is due to the template molecule is not removed yet.

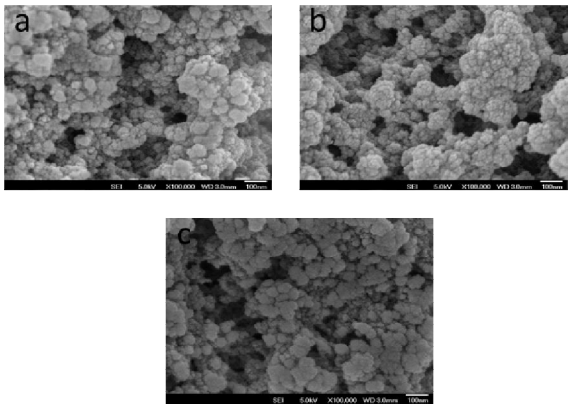


Fig.3. Field Emission Scanning Electron Micrographs of (a) MIP unleached, (b) MIP leached and (c) NIP.

3.2.4 EDX Analysis

Elemental analysis was carried out by Energy dispersive X-ray analysis to observe the percentage of carbon (C), silica (Si) and oxygen (O) element in NIP, MIP unleached and MIP leached tabulated in table 3.

Table 3. Percentage of carbon, silica and oxygen in molecularly imprinted polymer.

Sample	Percentage by Mass		
	Carbon	Silica	Oxygen
NIP	37.67	62.33	-
MIP unleached	37.12	62.04	0.84
MIP leached	39.87	60.13	-

The result showed that the presence of oxygen in MIP unleached can be considered from template molecule (o-cresol) at OH molecule. However, for NIP and MIP leached no percentage of oxygen detected. It mean that o-cresol as a template was totally removed and leached out in MIP leached. In addition, for carbon and silica amount both result is parallel for each other except MIP leached demonstrated lower amount of silica and high amount of carbon.

3.3 Binding properties of MIP and NIP

3.3.1 Effect of solid-liquid ratio and adsorption capacity

The effect of solid-liquid ratio on the adsorption capacity of MIP and NIP were studied by varying polymer weight (10-50 mg) in 10 mL of 2 mg/L o-cresol standard. The adsorption results under different solid-liquid ratio condition were given in Fig. 4. As seen clearly, MIP possessed strong adsorption ability when its dry weight was 30 mg, which illustrated maximum adsorption capacity was attained with certain dosage of the polymer. However, for lower sorbent dosages the adsorption capacity increased gradually and became static after 30 mg weight of sorbent. Therefore, 30/10 (w/v, mg mL^{-1}) was chosen as the optimum solid-liquid ratio in experiments.

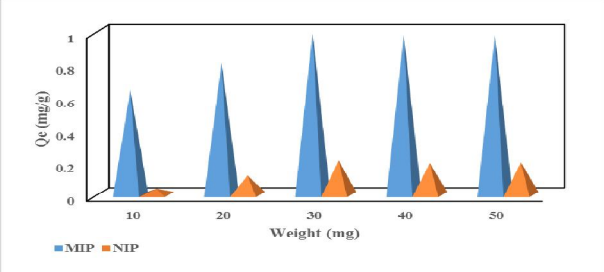


Fig. 4. Adsorption properties in five different solid-liquid ratios.

3.3.2 Effect of pH on adsorption capacity

Hydrogen ions concentration in the adsorption process was always considered as one of the most important parameters that influence the adsorption behavior of analytes in aqueous solution. The effect of pH on o-cresol loading capacity of MIP and NIP were studied by varying initial pH levels between 4.0 to 9.0. As demonstrated in Fig. 5, the adsorption capacities of MIP and NIP were not dependent on the equilibrium pH because in remain slightly the same on all pHs. The adsorption capacities increased gradually until it reached the maximum amount at pH 6.0 and continued decreasing slowly. O-cresol is protonated in neutral and alkaline medium. The acidic pH resulted the higher adsorption capacities because of more hydrogen bonds formed between $=CH_2$ from 3-PMTMOS and the active groups hydroxyl in o-cresol.

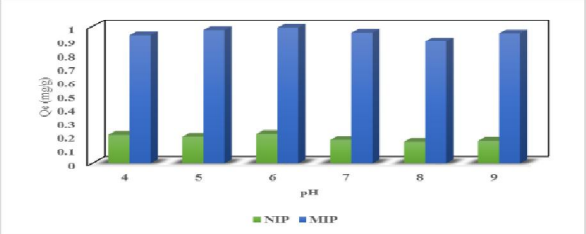


Fig. 5. Function of pH values on equilibrium adsorption amount.

3.3.3 Adsorption isotherm

The experimental equilibrium isotherm of o-cresol bound to MIP and NIP with different initial concentrations is demonstrate in Fig. 6. It could be seen that the amount of o-cresol absorbed in the polymers increased along with increasing the initial o-cresol concentrations at the beginning of adsorption and this might be the reason that the amount of o-cresol was not enough to saturate the specific binding cavities. When the concentration of o-cresol went up to 2.0 mg/L, the adsorption capacities remained stable with the maximum adsorption capacity of 0.991 mg/g for MIP which indicated that a many o-cresol specific binding sites were produced during imprinting process. In spite of that, Fig. 6 also showed that the amount of o-cresol bound to the MIP were in a high level compared with those of the NIP under the same conditions.

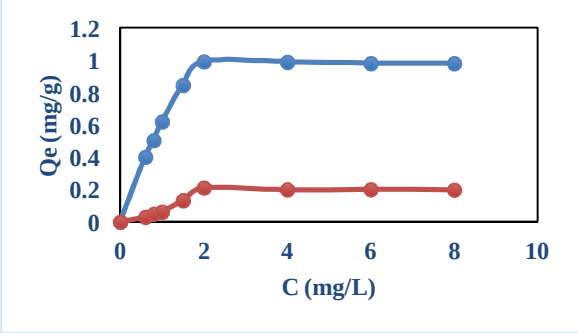


Fig. 6. Adsorption isotherm of MIP and NIP toward o-cresol.

Fig. 7 (a) demonstrated the chromatogram of remaining solution after being adsorbed by NIP while fig. 7 (b) illustrated the chromatogram of remaining solution after being adsorbed by MIP. This chromatogram indicates that no peak o-cresol was found because of MIP successfully adsorb all of the analyte. On the other hand, Fig. 7 (b) shows o-cresol peak still appeared on the chromatogram. So, this indicates that NIP only adsorb small amount of o-cresol.

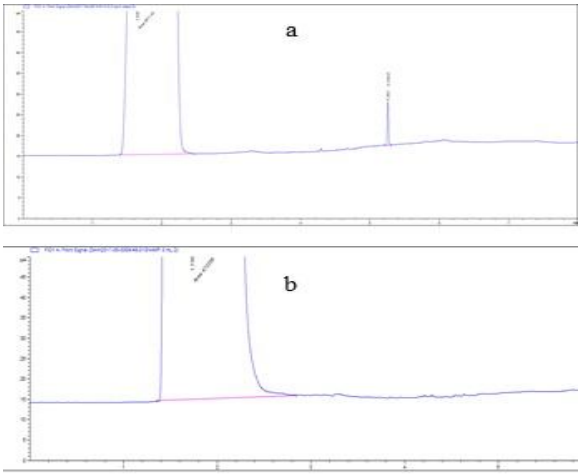


Fig 7. Chromatogram of (a) the remaining solution after adsorbed by NIP (b) and MIP.

CONCLUSION

A molecularly imprinted polymer of o-cresol was successfully prepared and synthesized. This material was synthesized using o-cresol as the template molecule, 3-PMTMOS as the monomer, ethanol as the porogenic solvent and TEOS as the cross-linker via sol-gel polymerization. Hydrogen bond and Van der Waals interaction play as the vital recognition cavity in this material. The optimum condition in preparation and synthesize MIP using 800 µL 3-PMTMOS. The prepared polymers were evaluated by a series of adsorption experiment, extraction experiment, FTIR, BET and FESEM-EDX analyses. Furthermore, the imprinted polymer which demonstrated the excellent adsorption properties and applicability will be used as the sorbent pack for solid phase extraction for the determination of o-cresol in urine sample.

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