Synthesis and Characterization of Chitosan Linked by Methylene Bridge and Schiff Base of 4,4-Diaminodiphenyl Ether-Vanillin

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ABSTRACT

The synthesis chitosan-methylene bridge-Schiff base of 4,4-diaminodiphenyl ether-vanillin using casting method has been done. The aims of this research were modification chitosan with Schiff base of 4,4-diaminodiphenyl ether-vanillin, formaldehyde and its characterization using FTIR spectroscopy, SEM analysis, ^{1}H–NMR and X-Ray Diffraction analysis. The first step was a synthesis of modified chitosan between chitosan and Schiff base of 4,4-diaminodiphenyl ether-vanillin. The second step was chitosan modified Schiff base of 4,4-diaminodiphenyl ether-vanillin then reacted with formaldehyde through casting method. The result showed that chitosan can be modified with Schiff base of 4,4-diaminodiphenyl ether-vanillin and formaldehyde and this modified chitosan can be linked by methylene bridge (–NH–CH_2–NH–) and had azomethine group (–C=N–). The functional group of –C=N in modified chitosan before and after adding formaldehyde appeared at a constant wavenumber of 1597 cm^{-1}. The functional group C–N in methylene bridge detected at 1388 and 1496 cm^{-1}. The chitosan-Schiff base of 4,4-diaminodiphenyl ether-vanillin and Chitosan-methylene bridge-Schiff base of 4,4-diaminodiphenyl ether-vanillin had index crystalline (%)16.04 and 25.76, respectively. The chemical sift of signal proton azomethine group (–C=N–) in modified chitosan detected at 8.44–8.48 and 9.77 ppm. Proton from methylene bridge in modified chitosan appeared at 4.97–4.99 and 3.75 ppm. Surface morphology chitosan-methylene bridge-Schiff base of 4,4-diaminodiphenylether-vanillin had dense surfaces, mostly uniform and regular in shape.

Keywords: *chitosan; methylene bridge; Schiff base*

ABSTRAK

Telah dilakukan penelitian sintesis kitosan-jembatan metilen-basa Schiff 4,4-diaminodifenil eter-vanilin. Tujuan-tujuan dari penelitian adalah modifikasi kitosan dengan basa Schiff 4,4-diaminodifenil eter-vanilin, formalin dan karakterisasinya dengan menggunakan spektrofotomer FTIR, SEM, ^{1}H–NMR and XRD. Tahap pertama sintesa kitosan termodifikasi antara kitosan dan basa Schiff 4,4-diaminodifenil eter-vanilin. Tahap kedua kitosan termodifikasi basa Schiff 4,4-diaminodifenil eter-vanilin direaksikan dengan formalin melalui metode pencelupan (perendaman). Hasil penelitian menunjukkan bahwa kitosan dapat dimodifikasi dan kitosan termodifikasi ini dapat dihubungkan dengan jembatan metilena dan mempunyai gugus fungsi azometin (–N=CH). Gugus fungsi –N=CH dalam kitosan termodifikasi sebelum dan sesudah penambahan formalin mempunyai bilangan gelombang yang tetap yaitu 1597 cm^{-1}. Gugus fungsi C–N dalam jembatan metilena terdeteksi pada bilangan gelombang 1388 and 1496 cm^{-1}. Kitosan-basa Schiff -4,4-diaminodifenil eter-vanilin dan kitosan-jembatan metilena-basa Schiff 4,4-diaminodifenil eter-vanilin, masing-masing mempunyai indeks kristalinitas (%) 16,04 dan 25,76. Sinyal proton gugus fungsi azometin (–C=N–) di kitosan termodifikasi terdeteksi pergeseran kimianya pada 8,44–8,48 dan 9,77 ppm. Proton dari jembatan metilena di kitosan termodifikasi muncul pada 4,97–4,99 dan 3,75 ppm. Morfologi permukaan kitosan-jembatan metilen-basa Schiff 4,4-diaminodifenil eter-vanilin mempunyai permukaan yang padat, lebih seragam dan bentuk teratur.

Kata Kunci: *kitosan, jembatan metilen, and basa Schiff*

INTRODUCTION

Chitosan is a natural polymer, derived from chitin by alkaline deacetylation. Chitosan has chemical structure $(C_6H_{11}NO_4)_n$ (n = 1 and 3) and it has a mass of 161 g/unit monomer. The concentration of primary amine group (–NH_2) is 6.21 mmol/g if it is perfectly deacetylated [1]. The solubility of chitosan in dilute

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acidic aqueous solutions such as acetic, propionic, lactic, citric, and other acids and that is a problem of chitosan.

Chitosan can be modified by reaction substitution at $-NH_2$ group (C_2) and or –OH group (C_3, deacetylated unit) and (C_6, deacetylation unit). Kandile and Nasr [2] and Dai et al. [3] reported that the aims of chemical modification chitosan were to increase the metal adsorption properties and change the characteristic solubility of chitosan in water or acid medium. Modification $-NH_2$ group of chitosan can be carried out by two methods, i.e. physical and chemical method. Physical method is to increase widely of surface area, the active site of adsorption, swelling polymer chain, decrease crystallinity and to increase the swell of it. The chemical method can be done by grafting, impregnating and cross-linking [4].

Diamine monomer 4,4-diaminodiphenyl ether or 4,4-oxydianilline has two primary amine ($-NH_2$), with chemical formula of $C_{12}H_{12}N_2O$ and molecular weight 200.24 g/mol [5]. 4,4-diaminodiphenyl ether has one or more oxazine ring and called heterocyclic compound [6]. This primary amine can be modified to be derived 4,4-diaminodiphenyl ether and used in a biological and medical field [7].

Vanillin (3-methoxy-4-hydroxybenzaldehyde, IUPAC) obtained from vanilla pods is flavoring agent which used in industry such as food, drink and cosmetic [8]. Vanillin has chemical formula $C_8H_8O_3$ and molecular weight 152.15 g/mol [9]. Vanillin has an aromatic ring and it is trisubstituted with –CH=O, $-OCH_3$ and –OH groups [10]. Aldehyde group (–CH=O) can be reacted with primary amine from 4.4-diaminodiphenyl ether to form Schiff base (–N=CH–) group with mol ratio aldehyde and primary amine was 2:1 [11].

The solubility of chitosan only in dilute acidic aqueous solutions and it is a problem of chitosan so that chitosan need to modify. In this paper, we successfully synthesized Schiff base (–N=CH–) compound from aldehyde group of vanillin and one primary amine of 4,4-diaminodiphenyl ether with mol ratio aldehyde and primary amine were 1:1 to form Schiff base of 4,4-diaminodiphenyl ether-vanillin (compound 1). Another primary amine (as a free primary amine) at 4,4-diaminodiphenyl ether in compound 1 can be reacted with a primary amine of chitosan with formaldehyde compound as linkages [12-14] to form $-NH-CH_2-NH-$ group. This group acts as methylene bridge between chitosan and compound 1. The final product named chitosan-methylene bridge-Schiff base of 4,4-diaminodiphenyl ether-vanillin (compound 3) and the solubility properties of this product in dimethyl sulfoxide (DMSO) and N,N–dimethyl-formamide (DMF). If used as an adsorbent, compound 3 has functional groups of –NH–, –C=N– and –OH. Characterization of this product has been conducted based upon FTIR, XRD, ^1H–NMR and SEM data.

EXPERIMENTAL SECTION

Materials

Chemical were supplied from Merck and Aldrich in analytical grades such as acetic acid 100%, methanol, vanillin, dimethyl sulfoxide (DMSO), formaldehyde (37%, v/v), 4,4-diaminodiphenyl ether 97% and sulfuric acid 97% (v/v). Chitosan (DD 87%) obtained from CV. Ocean Fresh Bandung, West Java, Indonesia.

Instrumentation

The instruments used for characterization included Fourier Transform Infrared (FTIR) spectrometer (Shimadzu Prestige-21) for identifying the presence of functional groups. Scanning Electron Microscope (SEM) (JEOL JSM-6510 LA) for characterizing the surface morphology, ^1H–NMR spectrometer (JEOL JNM-ECP600) for characterizing the chemical structure using DMSO-d6 as a solvent, Fisher-Johns apparatus for analyzing of melting point and X-Ray diffractometer (Shimadzu XRD-6000) for evaluating the crystalline level.

Procedure

Synthesis Schiff base of 4,4-diaminodiphenyl ether-vanillin (compound 1)

Schiff base of 4,4-diaminodiphenyl ether-vanillin (Fig. 1) was synthesized according to Cucos et al. [11] procedure with slight modification. 4,4-diaminodiphenyl ether (4 g, 0.02 mol) was dissolved in 20 mL methanol in beaker glass 250 mL. In this beaker glass, vanillin solution (3.04 g, 0.02 mol, 10 mL methanol) was added. The mixture was stirred continuously at temperature 75 °C for 1 h. After 1 h, orange solution was appeared and stored at room temperature until yellow powder formed. The yellow powder washed with 10 mL methanol and dried in an oven at 55 °C until constant weight.

Synthesis chitosan–compound 1 (compound 2)

Chitosan (0.805 g, 0.005 mol) was dissolved with 20 mL acetic acid solution 3% (v/v) in beaker glass 250 mL and stirred continuously at room temperature for 30 min. After 30 min, clear chitosan solution formed. In this beaker glass was added compound 1 solution (5.010 g, 0.015 mol, 5 mL of DMSO). The mixture was stirred continuously at temperature 70 °C for 1 h. After 1 h, the mixture was transferred to the oven at temperature

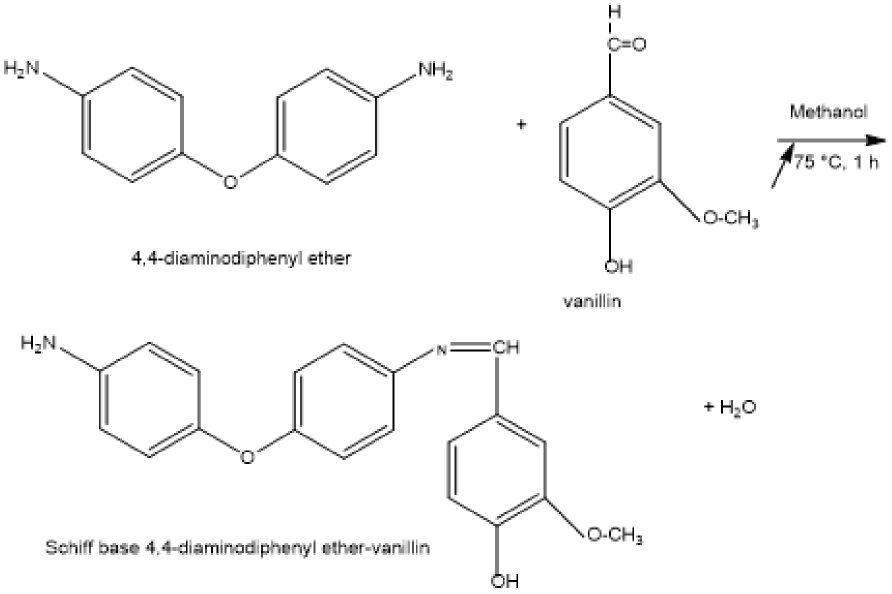

Fig 1. Illustration of chemical reaction of compound 1

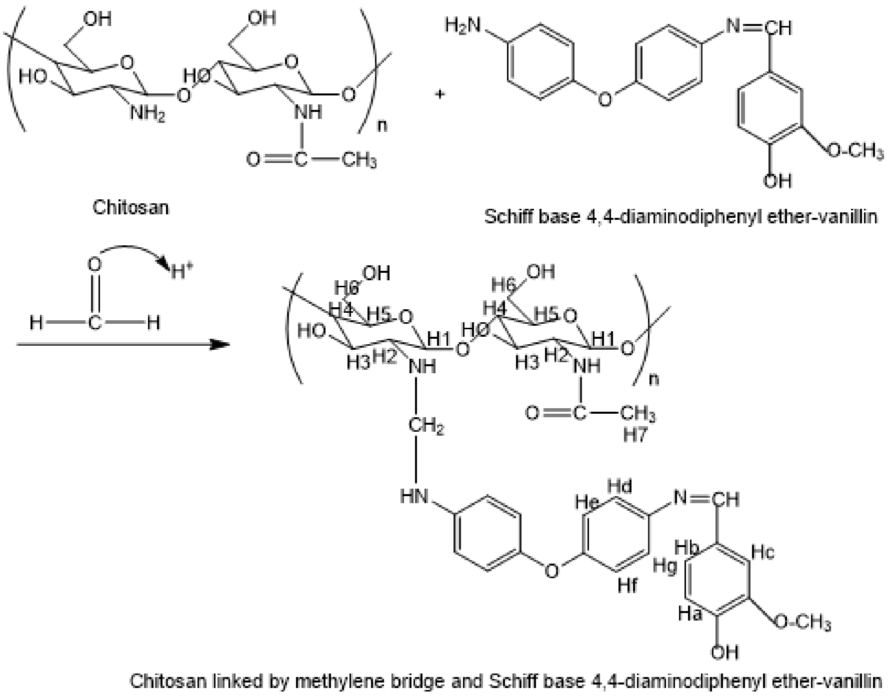

Fig 2. Schematic reaction of synthesis compound 3

70 °C until a brown gel formed. A brown gel washed with 10 mL ethanol and stored for 15 min at room temperature. A brown gel dried in an oven at temperature 50 °C until constant weight.

Synthesis chitosan linked by methylene bridge and compound 1 [12]

A 5 g of dry compound 2 was soaked in 5 mL of formaldehyde solution 37% (v/v) and 0.5 mL sulfuric acid solution 10% (v/v) in beaker glass 250 mL (Fig. 2). The mixture was stored at room temperature for 30 min. After 30 min, the mixture was washed with water several times until the filtrate has pH 6-7. The residue dried in an oven at 50 °C until constant weight. This product named chitosan-methylene bridge-Schiff base of 4,4 diaminodiphenyl ether-vanillin (compound 3).

Table 1. The result of melting point and solubility analysis

No.	Compound	Melting point (°C)	Solubility
1	4,4-diaminodiphenyl ether	187	methanol
2	vanillin	75	methanol
3	compound 1	125	DMF and DMSO
4	chitosan	230	Acetic acid
5	compound 2	80	DMF and DMSO
6	compound 3	160	DMF and DMSO

The functional group, morphology and physical structure analysis

Characterization of functional group, morphology and physical structure of chitosan before and after modification using FTIR spectroscopy, SEM analysis, and X-Ray diffractometer, respectively. The chemical structure of modified chitosan was identified using ^{1}H–NMR Spectroscopy.

RESULT AND DISCUSSION

Synthesis, Purification, Physical and Chemical Properties of Compound 3

4,4-diaminodiphenyl ether has two primary amines. The first, primary amine of 4,4-diaminodiphenyl ether can be reacted by aldehyde group of vanillin to get compound 1 and it has azomethine group (–N=CH). Unreacted aldehyde purified with methanol in compound 1 product. The second, primary amine of 4,4-diaminodiphenyl ether at compound 1 is free of primary amine and can bound with primary amine chitosan with formaldehyde as linkages to form compound 3.

The purification of compound 2 with absolute ethanol to remove acetic acid whereas the purification of compound 3 using distilled water to remove excess of formaldehyde and neutralization process of this product, so it will increase in coordination ability of hydroxyl oxygen atom and basicity of the imine nitrogen atom as active sites [15]. Fajardo et al. [12] and Li et al. [13] used formaldehyde as linkage and reported that chitosan structure after modified had the reactive functional group N and S as donor atom. We synthesized modified chitosan had the reactive functional group of $–NH_2$, –NH–, azomethine group and hydroxyl oxygen atom (phenolic groups) [15-17]. If it's used such at adsorption process, the reactive functional group N and O can act as donor atom because decreases effect of the electron density at the phenolic oxygen atom and modified chitosan contain the electron cloud upon the aromatic ring and the electronegative atoms such as nitrogen and oxygen [15].

The analysis of physical (melting point) and chemical properties (solubility) compound 1, 2, and 3 as seen in Table 1. Table 1 showed that the melting point of compound 3 was higher than compound 1 and 2.

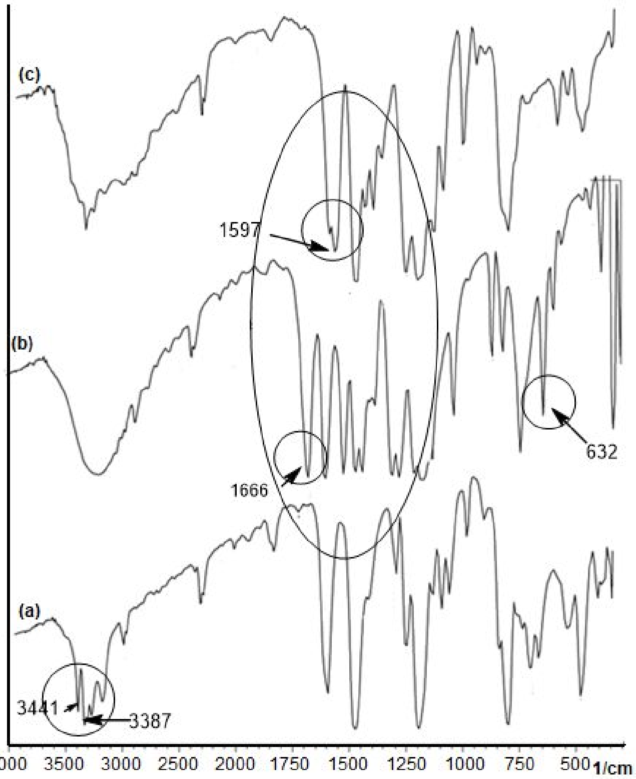

Fig 3. The FTIR spectra of: (a) 4,4-diaminodiphenyl eter, (b) vanillin, and (c) compound

Characterization of Product Synthesis

Presence of functional group with FTIR

Synthesis of compound 1. The reaction between aldehyde group (vanillin) and primary amine (4,4-diaminodiphenyl ether) formed Schiff base compound with mol ratio (aldehyde and primary amine group) 1:1. The spectra FTIR vanillin, 4,4-diaminodiphenyl ether and compound 1 are shown in Fig. 3.

The FTIR spectra of 4,4-diaminodiphenyl ether (Fig. 3a) shows that peaks at 3441 and 3387 cm^{-1} are as asymmetric and symmetric stretching vibration of primary amine ($–NH_2$) respectively [18-19]. Stretching vibration of C–O (C–O–C) appeared with a sharp peak at 1219 cm^{-1} and a medium peak at 1087 cm^{-1} and 1010 cm^{-1} [20-21]. Bending vibration N–H from primary amine appeared at wavenumber 1620 cm^{-1} with a

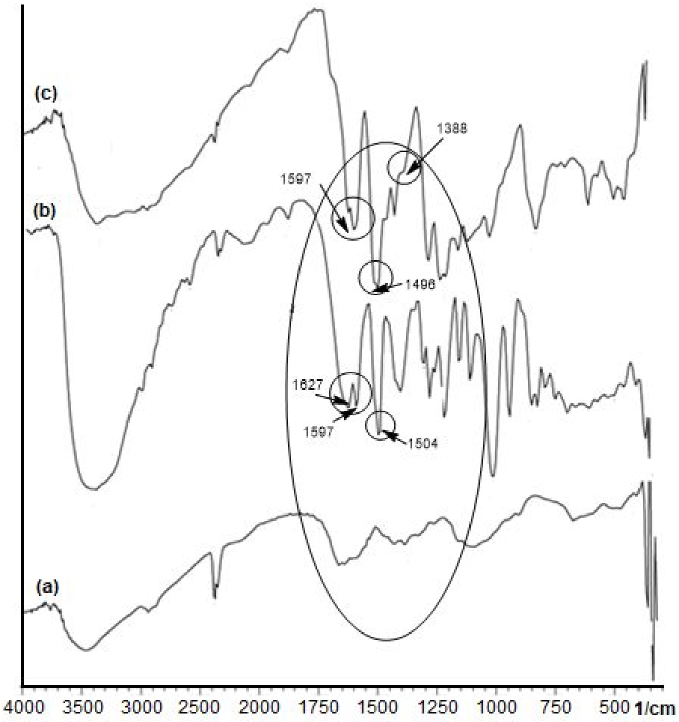

Fig 4. FTIR spectra of: (a) chitosan, (b) compound 2, and (c) compound 3

sharp peak and a peak at 1273 cm^{-1} with medium intensity is assigned stretching vibration of C–N from aromatic amine (NH$_2$-Aromatic) [20]. Stretching vibration of the aromatic ring (C=C–C) detected with a weak peak at 1442 cm^{-1} and a sharp peak at 1504 cm^{-1}, whereas stretching and bending vibration of C–H aromatic ring appeared at wavenumber between 3016–3039 cm^{-1} and 732-825 cm^{-1}, respectively [20-21].

The FTIR spectra of vanillin (Fig. 3b) shows that stretching (a broad band) and bending (a medium band) vibration –OH group are detected at 3178 and between 1265–1296 cm^{-1}, respectively [22]. Stretching vibration –C–H can be detected at 2847–3024 cm^{-1} with a weak band absorption. A sharp peaks at 1666 and 632 cm^{-1} are stretching and bending vibration of aldehyde group (C=O), respectively [10,22]. Stretching vibration of O–CH$_3$ with medium intensity appeared at 1026 cm^{-1} [10] and stretching vibration of C=C–C group appeared at wavenumber between 1427–1589 cm^{-1} [20-21].

Fig. 3c is the FTIR spectra of compound 1. In this spectra shows that a broad band at 3387 cm^{-1} are stretching vibration asymmetric of primary amine (N–H) and overlap with stretching vibration –OH, but –OH group also detected at 3224 cm^{-1} [18-20]. A peak at 1280 cm^{-1} is assigned as bending vibration of OH group [22]. Stretching and bending vibration of C–H group detected with weak and sharp peaks at 3008 and 833 cm^{-1}, respectively [10,21].

Stretching vibration of C=C–C group with a sharp intensity appeared at 1504 cm^{-1} [18]. Stretching vibration of C–O (C–O–C) appeared at 1226–1234 cm^{-1} (medium intensity) [21,23]. A peak at 1280 cm^{-1} with intensity medium is stretching vibration of C–N from aromatic amine (NH$_2$-Aromatic) [20]. Stretching vibration of O–CH$_3$ (medium intensity) appeared at 1033 cm^{-1} [10]. A new peak at 1597 cm^{-1} is a azomethine group (–N=CH–, Schiff base) [20,24-25].

Synthesis of compound 3. The FTIR spectra chitosan, compound 2 and compound 3 were shown in Fig. 4. The FTIR spectrum of chitosan (Fig. 4a) shows that a peak at 3441 cm^{-1} representing –OH stretching and overlap with –NH stretching vibration [26-27]. The weak band at 2924 cm^{-1} attributed to –CH and –CH$_2$ stretching vibration of chitosan [26-27]. The characteristic of at 1604 cm^{-1} is due to bending vibration of primary amine chitosan [27-28]. C–H symmetric bending vibrations in –CHOH– appeared at 1381 cm^{-1} [29]. –NH deformation vibration in primary amine can be found at 1427 cm^{-1} [25] and a peak at 1095 cm^{-1} is stretching vibration of C–O group [17].

The FTIR spectrum of compound 2 (Fig. 4b) had a peak at 3387 cm^{-1} and it is stretching vibration –OH group [20] from chitosan and vanillin. This –OH group overlaps with –NH primary amine in chitosan and 4,4-diaminodiphenyl ether. The bending vibration of –NH primary amine from chitosan and 4,4-diaminodiphenyl ether appeared with medium intensity at 1627 cm^{-1}, bending vibration OH group observed at 1226-1311 cm^{-1}, a peak at 2916 cm^{-1} is stretching vibrations of –CH and –CH$_2$ and the functional group of C=C–C (stretching vibrations) appeared at 1411 and 1504 cm^{-1} [20]. A peak at 1118 cm^{-1} (C–O–C group) is stretching vibrations [20] from chitosan and 4,4-diaminodiphenyl ether. The stretching vibration of –OCH$_3$ vanillin appeared at 1018 cm^{-1} [10]. Absorption band observed at 1597 cm^{-1} is due to the vibration stretch of Schiff Base (–N=CH–) group [20,24-25] from the reaction between aldehyde group of vanillin and one primary amine group of 4,4-diaminodiphenyl ether. The data from FTIR spectra in Fig. 4b shown that compound 2 has functional groups of –NH$_2$, –C=N– and –OH.

The FTIR spectrum of compound 3 (Fig. 4c) shows that stretching vibration –OH (at chitosan and vanillin) with broad band appeared at 3324–3363 cm^{-1} and bending vibration OH group observed at 1211–1234 cm^{-1} (medium intensity) [20]. Kandile et al. [17] reported that a peak at 3363 cm^{-1} was the functional group –NH secondary. A peak at 1118 cm^{-1} (C–O–C group) is stretching vibrations [20] from chitosan and 4,4-diaminodiphenyl ether whereas the stretching vibration of $–OCH_3$ vanillin appeared at 1026 cm^{-1} [10].

A new peak at 1388 cm^{-1} with weak intensity appeared after added formaldehyde. Monier [14] and Du et al. [30] reported that this peak was C–N group from methylene bridge ($–NH–H_2C–NH–$). In other hand, after added a formaldehyde the functional group of C=C–C (stretching vibrations) appeared at 1427 (medium intensity) and 1496 cm^{-1} (sharp intensity) but a peak at 1496 cm^{-1} is also C–N group from methylene bridge ($–NH–H_2C–NH–$) and this peak obscured of C=C–C group in benzene ring as reported by [31-33]. The wavenumber of 1597 cm^{-1} (–N=CH– group) was constant and this peak was almost not affected by adding formaldehyde whereas bending vibration of –NH primary amine from chitosan and 4,4-diaminodiphenyl ether at 1627 cm^{-1} were disappeared. This fact showed that formaldehyde was reacted with $–NH_2$ group [12-14,25] in chitosan ($–C_2–NH_2$) and 4,4-diaminodiphenyl ether ($–C–NH_2$) become –C–N– group as methylene bridge. The data from FTIR spectra in Fig. 4c shown that compound 3 has the functional group of the secondary amine (–NH–), –C=N– and –OH.

Analysis of physical structure with XRD

The physical structure of chitosan, compound 2 and 3 can be seen in Fig. 5. Fig. 5a shows that physical structure of chitosan is crystalline form. It has two strong diffractions at 2θ = 9.90° and 20°. These peaks are corresponding to the characteristics of chitosan [27,34]. The crystalline form chitosan is an indication that chitosan structure has intra and intermolecular hydrogen bond included all polymer chain.

Diffraction of chitosan modified as shown in Fig. 5b and c have changed the crystallinity of chitosan. This fact showed that strong hydrogen bond in chitosan can be deformed by insertion of the functional group [35-36] Schiff base of 4,4-diaminodiphenyl ether-vanillin. The index of crystalline (%) of chitosan, compound 2 and 3 were 50.50, 16.04, and 25.76, respectively.

Analysis of chemical structure with ^{1}H–NMR

^{1}H–NMR spectra of compound 2 and 3 are shown in Fig. 6 and Fig. 7, respectively. DMSO-d$_6$ used as a solvent in order to identify the chemical structures of compound 2 and 3.

As can be seen in Fig. 2 and 6, the signals of proton H_a, H_b and H_c vanillin were observed at 7.04–7.06 (d), 7.20–7.21 (d) and 7.49 (s) ppm, respectively [36]. A signal at 3.83–3.84 (s) ppm was proton of $–OCH_3$ in vanillin [38] and signal proton of –OH appeared at 6.76–6.78 ppm (d) [39].

Protons of 4,4-diaminodiphenyl ether were observed at different region (signal). A signal at 6.50–6.52 ppm (d) was H_d proton (meta) and signal appearing at 6.58–6.62 ppm (dd) may be due to H_e proton (ortho) [40-41]. Protons of H_g (meta) and H_f (ortho) can be found at chemical shift 7.27–7.31 ppm (dd) [42] and 6.86–6.88 ppm (dd) [21,43], respectively. Proton from azomethine (–N=CH–) group appeared at 8.43–8.44 ppm (s) [44].

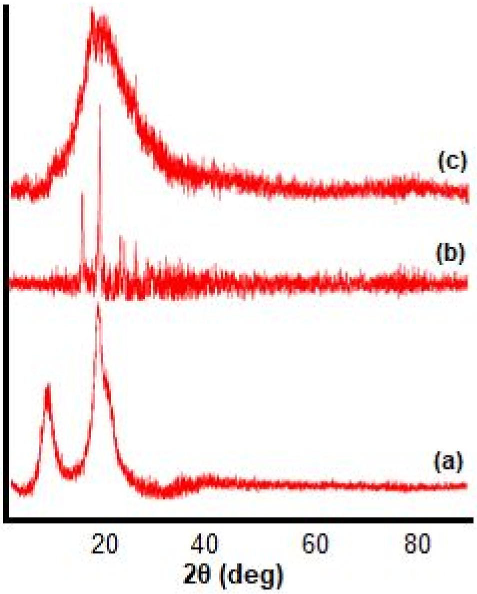

Fig 5. XRD powder patterns of: (a) chitosan, (b) compound 2, and (c) compound 3

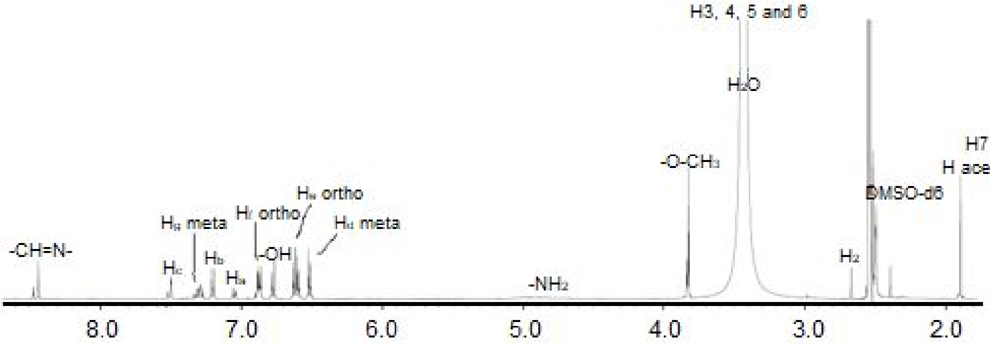

Fig 6. ^{1}H–NMR spectra of compound 2

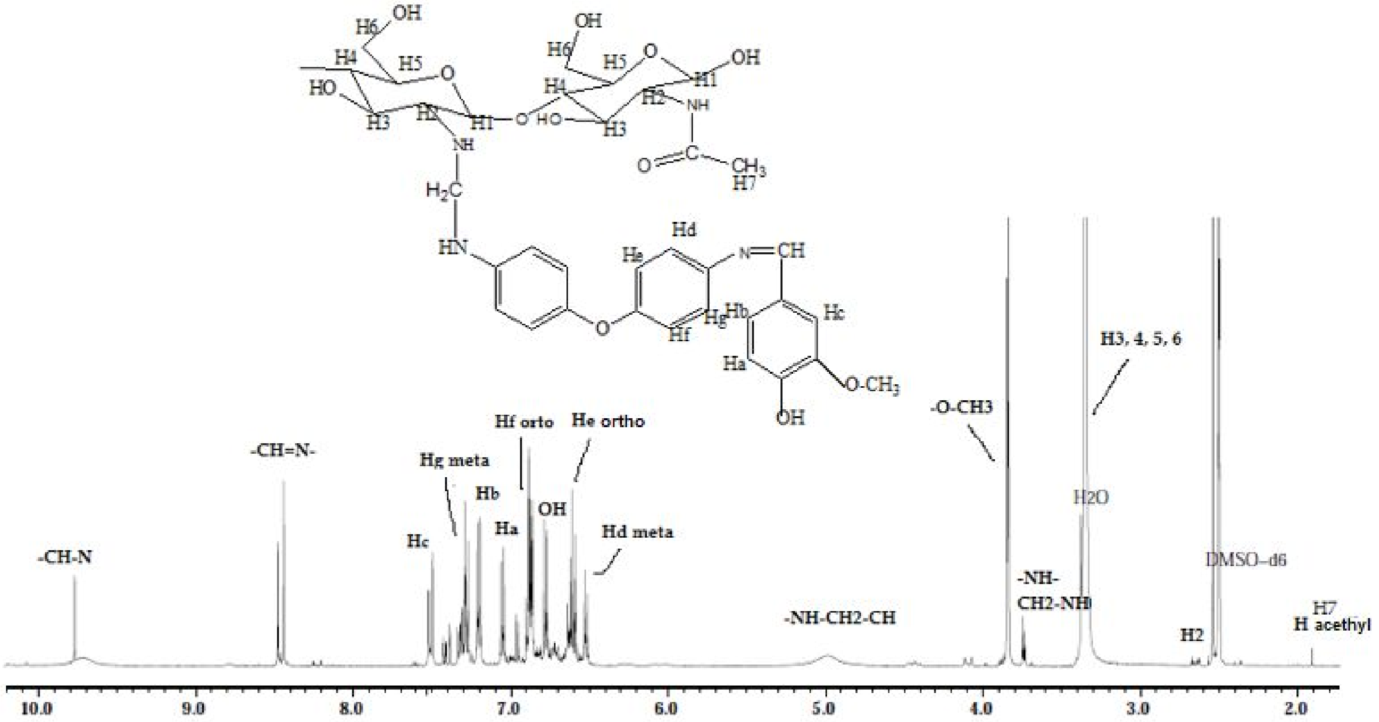

Fig 7. ^{1}H–NMR spectra of compound 3

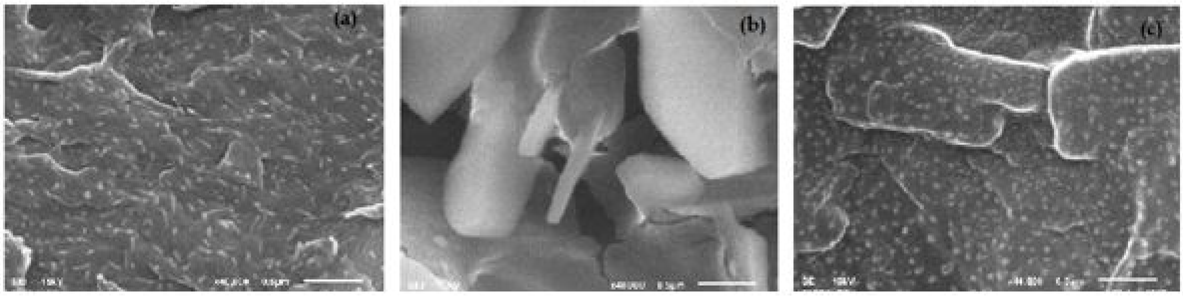

Fig 8. SEM image of: (a) chitosan, (b) compound 2 and (c) compound 3

H2 proton from chitosan was observed at 2.67 ppm (s) and the signal at 1.90 ppm (s) was shown as proton of H–acetyl [45]. H3, 4, 5, and 6 protons were not observable because they overlapped with a proton from H_2O [46] whereas $–NH_2$ proton was not detected as reported by Fang et al. [47]. The result of this analysis shown that there is a functional group of $–NH_2$ (although not detected), –C=N– and –OH in compound 2.

Fig. 7 show that there is a significant change in spectra of compound 3 compared to compound 2, so a new signals appeared and can be observed. A new signal of methylene bridge ($–NH–CH_2–NH–$) proton appeared in two regions and detected at chemical shift 4.97–4.99 (d) and 3.75 ppm (s) [39,48]. Proton from azomethine (–N=CH–) group was appeared become two signals, the first atchemical shift 8.44–8.48 ppm (s) [44] and the second at 9.77 ppm (s) [38]. The analysis of compound 3 with ^{1}H–NMR shown that only the functional group of primary amine ($–NH_2$) changed into secondary amine (–NH–).

The data from FTIR spectra in Fig. 4 shown that analysis of functional group was supported chemical structure of compound 2 and 3 (Fig. 2) which analyzed by ^{1}H–NMR (Fig. 6 and 7).

Analysis of surface morphology with SEM

Surface morphology chitosan, compound 2 and 3 are shown in Fig. 8. SEM image of chitosan (Fig. 8a) have surface morphology smooth and uniform [49-50]. If compared with Fig. 8b, the surface morphology of chitosan was changed. Surface morphology of compound 2 was not smooth and uniform but uneven and rough. As can be seen in Fig. 8c, surface morphology of compound 3 become regular in shape, had dense surfaces and mostly uniform.

CONCLUSION

Compound 3 was successfully synthesized by the reaction between chitosan, compound 1 and formaldehyde as linkages agent. The functional group of –CH=N– before and after addition formaldehyde was not changed. The presence of functional group C–N at methylene bridge can be detected at 1388 and 1496 cm^{-1}. The crystallinity of derivated chitosan was lower than raw chitosan. Proton methylene bridge was detected at 4.97–4.99 and 3.75 ppm, whereas proton azomethine (–N=CH–) appeared at 8.44–8.48 and 9.77 ppm. Surface morphology of derivated chitosan had shape uneven, rough, regular, dense surface and mostly uniform.

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