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Surface Modification of Multi-Walled Carbon Nanotubes with Polysaccharides

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Abstract. Multi-walled carbon nanotubes (MWCNTs) are known as efficient drug carriers. To improve their interaction with other materials, surface modification of MWCNTs is necessary. In this work, MWCNTs were functionalized with acid and polysaccharides (chitosan and gelatin). The functionalization process was done via modification with acid solutions of nitric acid, sulfuric acid, and a mixture of nitric acid-sulfuric acid first, followed by functionalization with chitosan and gelatin. To achieve the optimum condition of MWCNTs functionalization, the reaction time, temperature, and acid ratio were varied. Furthermore, the effect of chitosan and gelatin addition into MWCNTs was studied at various mass ratios. The synthesized materials were characterized by Fourier transform infrared spectrophotometer, Boehm titration, and dispersion test. The Boehm titration results showed that the acid functional groups had been attached successfully to MWCNTs surface. The amount of acid functional groups increased along with reaction time. The highest amount of acidic group obtained from the data was 2.33 mmol/g. It was achieved when MWCNTs reacted with nitric acid for 24 hours. Temperature and acid ratio variations on the MWCNTs functionalization did not provide significant results. From the FTIR data, sharp peaks at 3480 cm^{-1} and 1040 cm^{-1} indicates a -CONH bond, which shows that chitosan and gelatin have been successfully grafted onto MWCNTs surface via an amide linkage. Moreover, the dispersion test showed that the functionalized materials were stable for 48 hours.

Keywords: MWCNTs, Surface functionalization, Drug carrier, Polysaccharides, Chitosan, Gelatin

INTRODUCTION

Drugs are chemicals designed to prevent, provide therapeutic effects and cure a disease (Kwon et al., 2013). In conventional drug delivery systems, drug administration is done through oral, subcutaneous, and intravenous administration. The drug's effectiveness depends on the concentration at the target site. Conventional drug administration is considered less effective because it tends to have a short half-life in the body and low selectivity (Kwok et al., 2017). Nanomedicine could overcome this problem since it

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increases the half-life inside the body and the drug's selectivity. It can also increase bioavailability, reduce drug accumulation in normal tissues, and deliver drugs to specific tissues (Lombardo et al., 2019). Carbon nanotubes (CNTs) have been widely studied as alternative drug carriers in nanomedicine. CNTs have superior adsorbing properties due to their large surface area and their ability to form strong π-π electrostatic interactions. They have Enhanced Permeability and Retention Effect (EPR) properties that help deliver cancer drugs to tumor tissue. On top of that, CNTs also have a needle-like shape which allows for more effective penetration of target cells by passive diffusion through the lipid bilayer or endocytosis. To increase reactivity and active adsorption sites, the CNTs surface can be modified with various functional groups for further development in the medical field (Malek et al., 2019; Mahajan et al., 2018).

However, apart from the advantages mentioned above, CNTs have several disadvantages. For example, the usage of untreated CNTs poses a possible carcinogenic risk due to heavy metal residues. In addition, CNTs tend to be hydrophobic and can form agglomerates due to the relatively large Van der Waals forces between particles, which causes CNTs to have low dispersion ability and stability in liquids (Cirillo et al., 2014; Boncel et al., 2013; Datsyuk et al., 2008).

Surface modification of CNTs is a promising method to solve these problems. This method is used to attach acidic functional groups to the surface of CNTs. The attachment of acidic functional groups such as carboxyl (COOH), carbonyl (C=O), hydroxyl (OH), lactone, ketone, and anhydride must go through an oxidation reaction, which requires an oxidizing agent (Le Hoa et al., 2018). Oxidation reactions can be carried out with strong acids, such as nitric acid (HNO_3) and sulfuric acid (H_2SO_4). When reacted with CNT, the acid will oxidize the CNT surface wall and form defect sites for attachment of functional groups. Functional groups that are successfully attached to the CNT surface will change CNT's hydrophobic nature to hydrophilic, which improves their dispersion and stability.

Oxidized CNTs can be incorporated with biopolymers such as chitosan and gelatin to obtain better dispersion and stability properties. They can improve the dispersion properties and stability of MWCNTs since they act as surfactants and functionalize MWCNT non-covalently.

In this study, MWCNT nanocomposites were synthesized by oxidative treatment followed by grafting with chitosan and gelatin. The synthesized materials were analyzed using Boehm titration, FTIR, surface area analysis, TGA, and dispersion test.

MATERIALS & METHOD

Materials

Multi-walled carbon nanotubes (purity > 90%) were purchased from Cheap Tubes, USA. 65% nitric acid (HNO_3), 98% sulfuric acid (H_2SO_4), and 100% acetic acid glacial were purchased from Merck. Furthermore, low molecular weight chitosan and gelatin from bovine skin were purchased from Sigma Aldrich. All chemicals were used as received without further purification.

Surface Modification of MWCNTs

All methods in this study take the following research references conducted by Larasati (2021). The pristine MWCNTs (RAW) surface was modified with nitric acid and sulfuric acid mixtures. The modification was performed according to the following method: 500 mg of pristine MWCNTs were reacted with 100 mL of the acid solution for the temperature and treatment time study. The mixture was stirred with a hotplate stirrer for 6, 18, and 24 hours at various temperatures (40, 60, and 80^0C). To study the effect of volume ratio, pristine MWCNTs were reacted with mixtures of HNO_3 and H_2SO_4. The HNO_3 solution with a concentration of 14.4 M was combined with 10 M H_2SO_4 at different ratios (1:3, 1:5, 1:9) to create solutions with final volume of 100 mL. These mixtures were agitated for 6, 18, and 24 hours. After the modification process, the MWCNTs were washed several times with distilled water until the pH reached 6. Then, the modified samples (oxidized MWCNT or O-MWCNT) were dried at 50^0C overnight (Putri et al., 2020).

Boehm Titration

The Boehm titration method was used to determine the amount of oxygen functional groups on the surface of modified MWCNTs. In this experiment, 10 mg of modified MWCNTs were stirred in 50 mL of 0.05 M NaOH solution for 24 hours. Then, the mixture was filtrated and slowly titrated with 0.05 M HCl solution until it became neutral. The concentration of oxygen functional groups on MWCNTs surface was equal to the amount of reacted NaOH (Yuliantoro et al., 2021).

Grafting with Chitosan & Gelatin

Low molecular weight chitosan was homogenized in 100 mL acetic acid 1% (v/v) with an ultrasonication bath for 2 hours. In a separate beaker, one gram of oxidized MWCNTs was sonicated for 2 hours. Following that, both solutions were mixed, and the sonication was continued for another 4 hours. Glutaraldehyde 2.5% (3 mL) was added to the mixture when the sonication process was still in progress. After that, the mixture was centrifuged for 15 minutes at 4500 rpm. Then, the supernatant was washed several times with distilled water. The supernatant was centrifuged repeatedly until it reached pH 7. The solid material obtained was dried at 50^0C overnight.

Various amounts of gelatin from bovine skin were mixed with 50 mL of distilled water. The mixtures were stirred with a hotplate stirrer at 45^0C. Oxidized MWCNTs, 4% w/w, were mixed with ethanol 96% and stirred for 10 minutes. Both solutions were mixed, and the stirring continued for 1.5 hours. After that, The mixture was centrifuged for 15 minutes at 4500 rpm. Then, the supernatant was washed several times with distilled water. The supernatant was centrifuged repeatedly until it reached pH 7. The solid material obtained was dried at 50^0C overnight.

Table 1. Design Experiment of Chitosan & Gelatin Grafted MWCNTs

Sample	MWCNTs mass, mg	Chitosan/Gelatin mass, mg
CH-MWCNT1	1000	1000
CH-MWCNT2	1000	1500
CH-MWCNT3	1000	2000
CH-MWCNT4	1000	2500
GEL-MWCNT1	1006.25	240
GEL-MWCNT2	1006.25	360
GEL-MWCNT3	1006.25	480
GEL-MWCNT4	1006.25	600

MWCNTs Characterization

The synthesized materials were characterized by various methods. The functional groups on the surface of MWCNTs were identified by a Fourier transform infrared (FTIR) spectroscopy (Spectrophotometer Shimadzhu FTIR-8201

PC, Japan). To estimate the degree of functionalization and thermal stability, thermal gravimetric analysis (TGA) was performed on (TG/DTA Perkins Diamond Series). A small amount of MWCNTs (~3 mg) was scanned at a temperature range from 30^0C to 800^0C and a heating rate of 10 C/minute, under air. The total surface area and pore size of MWCNTs were analyzed using Brunauer-Emmett-Teller (BET) Nova 2000, Quantachrome (USA). A dispersion test was conducted to compare the stability of MWCNTs before and after functionalization. Four mg of MWCNTs were dispersed in 10 mL of demineralized water and sonicated for 5 minutes. The dispersions were observed for 48 hours.

RESULTS AND DISCUSSION

Surface Modification of MWCNTs Using Acids

Pristine MWCNTs were oxidized using nitric acid and sulfuric acid mixtures. Boehm titration was used to determine the concentration of the acidic functional group on MWCNTs after oxidative treatment. Oxidized MWCNTs were reacted with NaOH solution until they reached equilibrium, then titrated with HCl solution. The concentration of the acidic functional group (mmol/g MWCNTs) is equal to the difference in NaOH concentration before and after titration.

Influence of Treatment Duration

The influence of treatment duration on oxidized MWCNT can be seen in samples ABCD and NOPQ in Table 2. In samples ABCD, the nitric acid was used at its concentrated solution (14.4 M), while in samples NOPQ, the solution was diluted to 4 M. The total amount of acidic group in sample ABCD gradually increased for 24 hours and decreased after 48 hours. Samples NOPQ shows a similar trend as samples ABCD. The concentration of the acidic group in samples NOPQ increased for 18 hours and decreased for the next 48 hours, which happened due to the prolonged contact time with a strong acid. Prolonged oxidation will cause shortening to MWCNTs tubes, making the acid functional group unable to attach to its surface (Datsyuk et al., 2008). Despite that, samples ABCD produced a higher concentration of the acidic group than samples NOPQ. The difference in concentration was quite significant, from ± 0.3 mmol/g to ± 2 mmol/g.

Table 2. Influence of Treatment Duration on Acidic Group Concentration

Sample	HNO_3 Concen-tration, M	Treatment Time, hours	Acidic Group (mmol/g)
A	14.4	5	2.13
B	14.4	18	2.06
C	14.4	24	2.33
D	14.4	48	2.13
N	4	5	0.66
O	4	18	1.12
P	4	24	0.32
Q	4	48	0.00

Influence of Ratio of Nitric Acid and Sulfuric Acid Solution

Table 3. Influence of Acid Ratio on Acidic Group Concentration

Sample	HNO_3/H_2SO_4 Volume Ratio	Acidic Group (mmol/g)
H	1:3	1.14
I	1:5	0.94
J	1:9	1.09
L	1:3	0.81
M	1:3	2.17
K	1:3	0.97

From samples HIJ, the influence of acid ratio can be discovered. The acid concentration in these samples was 4 M for HNO_3 and 10 M for H_2SO_4. In these three samples, the concentration of the acidic group decreased as more H_2SO_4 was added. Since this study used a diluted HNO_3 and H_2SO_4 mixture, the produced mixture was not strong enough to create defect sites in the MWCNTs surface, so only a few acidic groups managed to attach to the MWCNTs surface.

The effect of adding H_2SO_4 solution on the oxidative treatment of MWCNTs can be observed from samples NOPQ and HLMK. The NOPQ samples were treated with diluted HNO_3 (4 M), while the HLMK were treated with a mixture of HNO_3 (4 M) and H_2SO_4 (10 M). From the information in Table 3, the samples HLMK show greater acidic group concentration.

At 48 hours, the increase in acidic concentration was quite significant. Sample K produced a concentration of 2.17 mmol/g, while the concentration for NOPQ ranges from ±0.3-1.1 mmol/g. Since sulfuric acid is a strong acid that can oxidize the MWCNTs surface efficiently, it can be concluded that the addition of strong acid as oxidative treatment of MWCNTs produces a greater concentration of acidic groups.

Influence of Treatment Temperature

Table 4. Influence of Treatment Temperature on Acidic Group Concentration

Sample	HNO_3 Concentration, M	Treatment Temperature, ^{0}C	Acidic Group, mmol/g
E	14.4	40	1.63
F	14.4	60	1.47
G	14.4	80	1.63

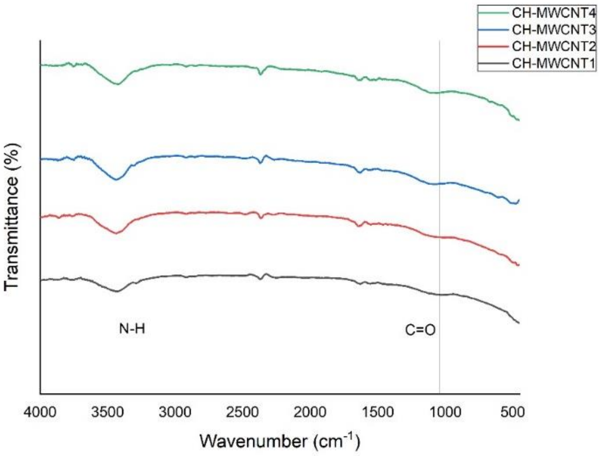

Fig. 1: FTIR Spectra of RAW and O-MWCNT

The effect of temperature on the modification of MWCNTs can be observed in EFG samples. These samples were treated with concentrated HNO_3 (14.4 M) at temperatures of 40, 60, and 80^{0}C. The result is that the concentration of the acidic group from EFG samples tends to be constant. Sample F slightly decreased compared to sample E (1.63 mmol/g decreases to 1.46 mmol/g). At 80^{0}C, the acidic concentration rose back to 1.63 mmol/g. These results show that the temperature variation in this oxidative treatment did not produce a significant result in acidic concentration. From the results of Boehm titration, it can be deduced that sample C yields the largest concentration of acidic groups, which is 2.33 mmol/g.

Grafting of Oxidized MWCNTs Using Chitosan & Gelatin

Fourier Transform Infrared (FTIR)

FTIR analysis was used to determine the existence of specific functional groups in a material. Figures 1, 2, and 3 below show FTIR spectra of RAW, O-MWCNT, CH-MWCNT, and GEL-MWCNT.

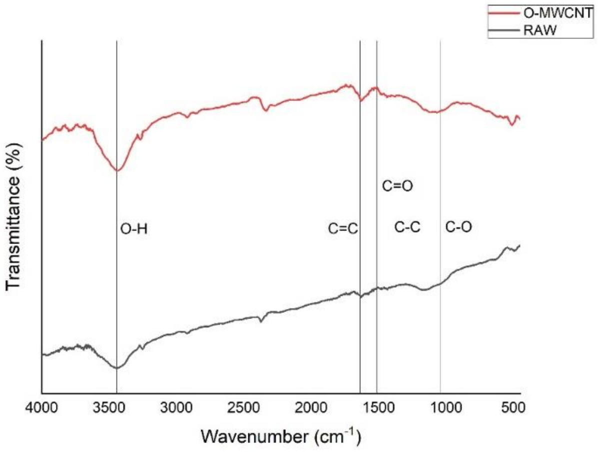

Fig. 2: FTIR Spectra of CH-MWCNT

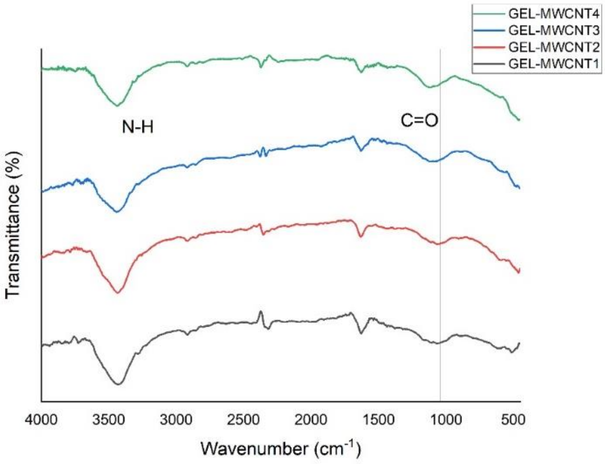

Fig. 3: FTIR Spectra of GEL-MWCNT

Figure 1 shows FTIR spectra of pristine MWCNTs (RAW) and oxidized MWCNTs (O-MWCNT). Based on the image, characteristic peaks for the RAW sample are seen at a wavenumber of 1630 cm$^{-1,}$ which attributes to the existence of the C=C bond on MWCNTs. Whereas peak 1160 cm^{-1} shows the presence of C-C bonds (Saleh et al. 2011). The peaks at 1537 cm^{-1} and 1040 cm^{-1} were caused by the vibration of C=O and C-O (Sobh et al., 2019). In the O-MWCNT sample, the peak at 1630 cm^{-1} indicates a C=C bond with a deeper peak. This peak intensity increased due to the structural damage of MWCNTs symmetry resulting from oxidative treatment. It caused the onset of electric dipole force, which resulted in the emergence of the peak. Furthermore, the peak at 1120 cm^{-1} is related to C-O bond stretching. A deeper peak at 3440 cm^{-1} shows the vibration of -OH groups (Aslani et al., 2017). Since the acid groups was successfully attached to MWCNT's surface, this result indicates that oxidative treatment would sharpen the peak.

The spectra of CH-MWCNT samples are shown in Figure 2. In these four samples, there were intense peaks at 3448 cm^{-1} and 1040 cm$^{-1,}$ which appear due to stretching vibrations of N-H and C=O in the -CONH bond, confirming that chitosan has been successfully grafted onto MWCNTs surface via amide linkage (Sobh et al., 2019). The GEL-MWCNT samples also gave similar results, as shown in Figure 3. All GEL-MWCNT samples had similar peak characteristics at 3448 cm^{-1} and 1040 cm^{-1}. GEL-MWCNT3 and GEL-MWCNT4 samples underwent a slight shift for the C=O bond. These GEL-MWCNT3 and GEL-MWCNT4 peaks shift to 1090 cm^{-1} and 1080 cm^{-1}, respectively. Therefore, gelatin was also successfully grafted onto MWCNTs surface.

Thermal Gravimetric Analysis (TGA)

Table 5. Total Weight Loss of MWCNTs

Sample	Total Weight Loss, %
RAW	7
O-MWCNT	20
CH-MWCNT1	34
CH-MWCNT2	32
CH-MWCNT3	60
CH-MWCNT4	29
GEL-MWCNT1	24
GEL-MWCNT2	28
GEL-MWCNT3	37
GEL-MWCNT4	23

Thermal gravimetric analysis is a simple method to study the decomposition pattern and thermal stability of MWCNTs nanocomposites. The operating condition was set at the range of 500-800^{0}C with a heat flow rate of 10^{0}C/minute under air (Le Hoa et al., 2018).

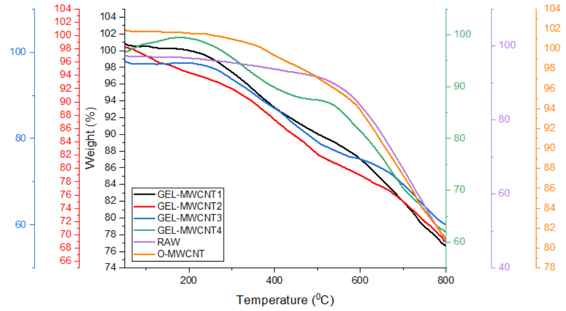

Fig. 4: TGA Curve of CH-MWCNT

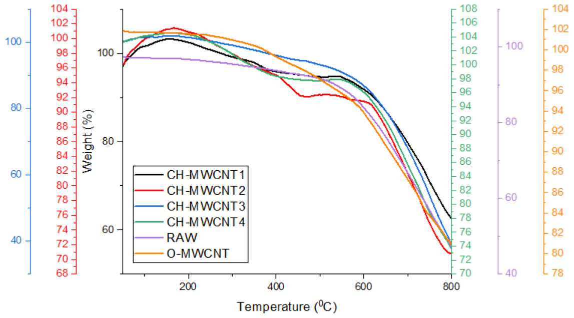

Fig. 5: TGA Curve of GEL-MWCNT

Figures 4 and 5 show that RAW sample lost 7% of total weight at 800^{0}C, which indicates that the RAW sample was pure and there were no defect sites on its surface. On the other hand, the MWCNTs samples, which have been oxidized with acid (O-MWCNT), had a total weight loss of 20% at 800^{0}C. Oxidative treatment using acid caused shortening in MWCNTs structure and created defect sites on its surface, resulting in a more significant weight loss (Carson et al., 2009).

In a series of CH-MWCNT samples, the most significant weight loss of 60% was by CH-MWCNT3 sample, followed by CH-MWCNT1, CH-MWCNT2, and CH-MWCNT4. Higher total weight loss of the sample means that more amine groups of chitosan have been attached successfully to the MWCNTs surface. From Table 3, it can be observed that the CH-MWCNT3 sample has the most significant amount of grafted chitosan. In general, at temperatures between 210-450^{0}C, there was a significant weight loss caused by the decomposition of chitosan. At this temperature, the amide group formed inside the MWCNTs surface was damaged, thus resulting in a significant weight loss (Hsan et al., 2020). The subsequent significant weight loss occurred at the temperature range of 600-800^{0}C. This weight loss was due to the oxidative removal of glycosidic bonds of chitosan (Carson et al., 2009).

For GEL-MWCNT samples, from Table 5, it can be observed that the GEL-MWCNT3 sample lost the most weight at 37%. The other samples lost 24, 28, and 23% weight for GEL-MWCNT1, GEL-MWCNT2, and GEL-MWCNT4. These results show the same conclusion as the TGA curve from CH-MWCNT samples: As more gelatin chains have been successfully grafted on MWCNTs surface, the greater the weight loss of the sample will be. Overall, the weight loss at temperatures from 250-450^{0}C was attributed to the partial breaking of gelatin molecular structure. While at 450-800^0, the weight loss was attributed to the combustion of remaining gelatin and chemical degradation resulting from broken chemical bonds in the gelatin polymer chains (Sharmeen et al., 2018).

Furthermore, the CH-MWCNTs samples gave higher total weight loss than GEL-MWCNT samples, meaning more chitosan was successfully grafted on MWCNTs surface than gelatin. Figures 4 and 5 also provide information about thermal stability. The lowest thermal stability was given by RAW, while O-MWCNT gave the best stability. CH-MWCNT and GEL-MWCNT samples also give better thermal stability compared to RAW.

However, these samples were less stable when compared to O-MWCNT. This is in accordance with a previous study that concludes that thermal stability for chitosan grafted MWCNT provides lower stability than the oxidized MWCNTs (Hsan et al. 2020).

Surface Area Analysis

Specific surface area characterization of MWCNTs was analyzed using Braun-Emmett-Teller (BET) method, while the pore radius was analyzed using Barret-Joyner-Halenda (BJH) method. The data obtained from this analysis are presented in Table 6.

Table 6. Surface Area Analysis of MWCNTs

Sample	Surface Area, m^2/g	Pore Radius, Å
RAW	91.82	27.06
O-MWCNT	96.16	26.94
CH-MWCNT1	73.54	27.39
CH-MWCNT2	71.89	27.34
CH-MWCNT3	73.04	26.62
CH-MWCNT4	70.86	26.89
GEL-MWCNT1	54.62	27.10
GEL-MWCNT2	50.77	27.27
GEL-MWCNT3	25.70	27.02
GEL-MWCNT4	41.47	435.05

Table 6 shows that the O-MWCNT sample (96.16 m^2/g) provides a larger surface area than RAW sample (91.82 m^2/g), while the pore size of O-MWCNT was smaller compared to RAW samples. The oxidation of MWCNT with acid produced defects and shortening inside the MWCNT structure which caused the surface area of the MWCNT to increase.

For CH-MWCNT, in general, the surface area decreases as more chitosan was grafted. The largest surface area was provided by the CH-MWCNT1 sample, at 73.54 m^2/g. Previous studies have shown that the surface area of pure chitosan was very low at 0.31 m^2/g (Hsan et al., 2020). In this study, with the addition of MWCNT, the surface area of the CH-MWCNT nanocomposite increased to ± 70 m^2/g. Thus, the surface area of CH-MWCNT was lower than O-MWCNT but significantly increased compared to pure chitosan.

The surface area of GEL-MWCNT samples also shows a similar trend with chitosan, with the largest surface area given by the GEL-MWCNT1 sample (54.62 m^2/g). It can be concluded that as more biopolymer is added to MWCNT, the surface area produced will be smaller. It could be because the concentration of the added biopolymer was too high, causing agglomeration of the MWCNT and uneven distribution of the biopolymer on the MWCNTs surface. This uneven distribution caused a decrease in surface area.

Dispersion Test

To obtain a good nanocomposite material as a drug carrier, a dispersion test is necessary to determine the dispersion and stability of the nanocomposite in the solvent. The result of the dispersion test conducted on all samples is shown in Figure 6 below.

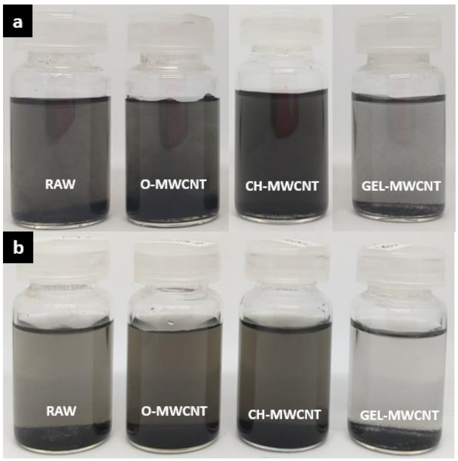

Fig. 6: Dispersion Test of MWCNTs

The dispersion test was observed for 48 hours. In Figure 6a, O-MWCNT and CH-MWNT give the best dispersion and stability after sonication. After 48 hours (Figure 6b), these two samples still had good dispersion and stability among the four samples. On the O-MWCNT sample, the oxidation process caused the attachment of the acidic group onto MWCNTs surface. This acidic group particle had the same charge, resulting in repulsions and causing the nanocomposite to be well dispersed inside the solutions. In addition, the CH-MWCNT sample also showed good stability when observed for 48 hours. The chitosan acted as a surfactant to increase MWCNTs solubility and functionalized MWCNTs non-covalently (Hsan et al. 2020). In contrast to RAW sample, which did not have an acidic group on its surface, the sample was not well dispersed and tended to settle quickly. The GEL-MWCNT sample also gave the same result as RAW sample. After 48 hours, GEL-MWCNT settled completely.

CONCLUSIONS

In this work, the characterization of modified MWCNTs using oxidative treatment and biopolymer were carried out. The MWCNTs were modified with nitric acid and sulfuric acid to obtain this aim. After that, the MWCNTs were grafted with chitosan and gelatin. The result obtained from Boehm titration indicates that MWCNTs treated with concentrated nitric acid at 24 hours give the highest acidic concentration, which is 2.33 mmol/g. The FTIR spectra show that chitosan and gelatin were successfully grafted onto MWCNTs surface. The decomposition pattern and thermal stability were investigated with TGA, which shows that oxidized MWCNT and chitosan/gelatin grafted MWCNTs give the best thermal stability. Surface area analysis using the BET method produces the best result for oxidized MWCNTs with a surface area of 96.16 m^2/g. Finally, the result of the dispersion test shows that oxidized and chitosan grafted MWCNT shows the best dispersion and stability for 48 hours. These results confirm that the surface modification on MWCNTs was successfully performed.

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REFERENCES

Aslani, M., Meskinfam, M., & Aghabozorg, H., 2017. "In Situ biomimetic synthesis of gelatin-carbon nanotube-hydroxyapatite biocomposites as bone filler", *Orient. J. Chem*, 33, 235-241.

Boncel, S., Zając, P. and Koziol, K.K., 2013. "Liberation of drugs from multi-wall carbon nanotube carriers", *Journal Control. Release*, 169(1-2), 126-140.

Carson, L., Kelly-Brown, C., Stewart, M., Oki, A., Regisford, G., Luo, Z., & Bakhmutov, V. I., 2009. "Synthesis and characterization of chitosan–carbon nanotube composites", *Mater. Lett.,* 63(6-7), 617-620.

Cirillo, G., Hampel, S., Spizzirri, U.G., Parisi, O.I., Picci, N. and Iemma, F., 2014. "Carbon nanotubes hybrid hydrogels in drug delivery: A perspective review", *BioMed Res. Inter.,* 2014, 825017.

Datsyuk, V., Kalyva, M., Papagelis, K., Parthenios, J., Tasis, D., Siokou, A., Kallitsis, I., and Galiotis, C., 2008. "Chemical oxidation of multi-walled carbon nanotubes", *Carbon,* 46(6), 833-840.

Hsan, N., Dutta, P. K., Kumar, S., Das, N., & Koh, J., 2020. "Capture and chemical fixation of carbon dioxide by chitosan grafted multi-walled carbon nanotubes", *J. CO2 Util.,* 41, 101237.

Kwon, S., Singh, R. K., Perez, R. A., Abou Neel, E. A., Kim, H.-W., dan Chrzanowski, W., 2013. "Silica-based mesoporous nanoparticles for controlled drug delivery", J. *Tissue Eng.,* 4, 204173141350335.

Kwok, Karl & Vincent, Erica & Gibson, James, 2017. Pharmacology and Therapeutics for Dentistry (7th edition): Antineoplastic Drugs, Elsevier.

Larasati, F. (2021). Kinetic and Isotherm Studies of Functionalized Multi-Walled Carbon Nanotube (MWCNT) with Biopolymer Variations as Drug Carrier [Master's thesis, Universitas Gadjah Mada]. ETD UGM: Theses and Dissertations Repository. http://etd.repository.ugm.ac.id/penelitian/detail/203068

Le Hoa, T.M., 2018. "Characterization of multi-walled carbon nanotubes functionalized by a mixture of HNO_3/H_2SO_4", *Diam. Relat. Mater.*, 89, 43-51.

Lombardo, D., Kiselev, M.A. and Caccamo, M.T., 2019. "Smart nanoparticles for drug delivery application: development of versatile nanocarrier platforms in biotechnology and nanomedicine", *J. Nanomater.,* 2019, 3702518.

Mahajan, S., Patharkar, A., Kuche, K., Maheshwari, R., Deb, P.K., Kalia, K. and Tekade, R.K., 2018. "Functionalized carbon nanotubes as emerging delivery system for the treatment of cancer", *Int. J. Pharm.,* 548(1), 540-558.

Malek, S.K., Gabris, M.A., Jume, B.H., Baradaran, R., Aziz, M., Abd Karim, K.J.B. and Nodeh, H.R., 2019. "Adsorption and in vitro release study of curcumin form polyethyleneglycol functionalized multi walled carbon nanotube: kinetic and isotherm study", *DARU J. Pharm. Sci.,* 27(1), 9-20.

Moore, T.L., Grimes, S.W., Lewis, R.L. and Alexis, F., 2014. "Multilayered polymer-coated carbon nanotubes to deliver dasatinib", *Mol. Pharm*., 11(1), 276-282.

Putri, R. G., Syafera, Y., Larasati, F., Putri, N. R. E., Handayani, M., & Kusumastuti, Y., 2020. "Effect of reaction time on modification of multi-walled carbon nanotubes with HNO_3". *IOP Conference Series: Mater. Sci. Eng.*, 742(1), 012038.

Saleh, T. A., 2011. "The influence of treatment temperature on the acidity of MWCNT oxidized by HNO_3 or a mixture of HNO_3/H_2SO_4", Appl. Surf. Sci., 257(17), 7746-7751.

Sharmeen, S., Rahman, A. M., Lubna, M. M., Salem, K. S., Islam, R., & Khan, M. A., 2018. "Polyethylene glycol functionalized carbon nanotubes/gelatin-chitosan nanocomposite: An approach for significant drug release", *Bioact. Mater.*, 3(3), 236-244.

Sobh, R. A., Nasr, H. E. S., & Mohamed, W. S., 2019. "Formulation and in vitro characterization of anticancer drugs encapsulated chitosan/multi-walled carbon nanotube nanocomposites", *J Appl Pharm Sci,* 9, 32-40.

Wong, B.S., Yoong, S.L., Jagusiak, A., Panczyk, T., Ho, H.K., Ang, W.H. and Pastorin, G., 2013. "Carbon nanotubes for delivery of small molecule drugs", *Adv. Drug Deliv. Rev.,* 65(15), 1964-2015.

Yuliantoro, H., Kusumastuti, Y., Mindaryani, A., Handayani, M., & Rochmadi., 2021. "Functionalization of single-walled carbon nanotubes with a HNO_3/H_2SO_4 mixture through different treatments: A DFT supported study", *AIP Conf. Proceed.,* 2349(1), 020071.