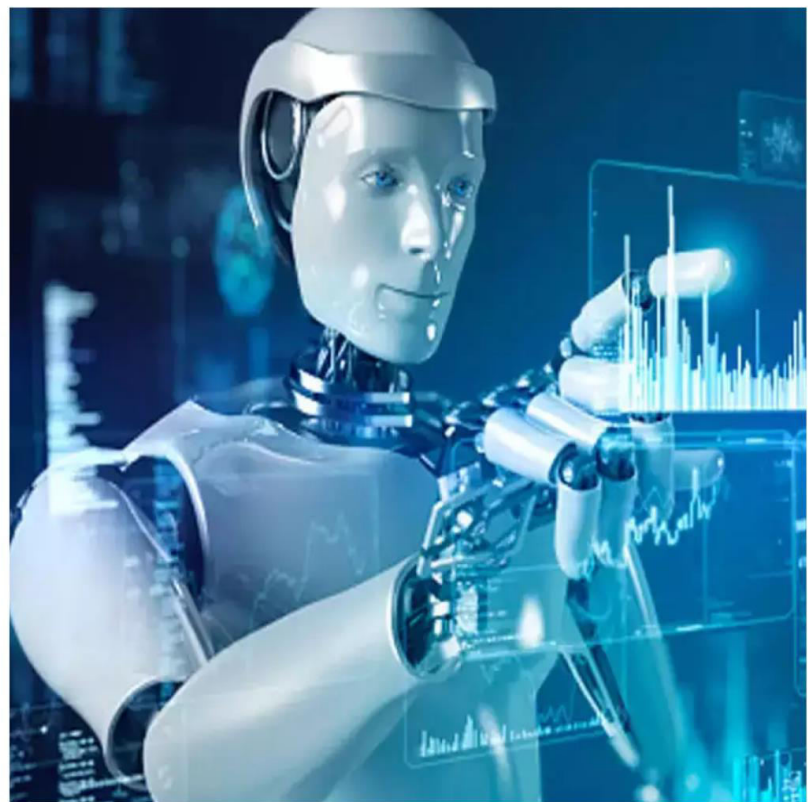




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# Development and Analysis of Carboxymethyl-Chitosan and Halloysite Nanotube-Based Bionanocomposite Films for Wound Care Applications

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**ABSTRACT:** This study aimed to develop chitosan derivative and halloysite nanotubes bionanocomposite films for biomedical applications especially for wound healing. Firstly, water-soluble chitosan derivative i.e. carboxymethyl-chitosan (CMCS) was synthesized via carboxylation reaction. Then, stock solution of CMCS (w/v %) and halloysite nanotubes (w/v %) were prepared separately in distilled water. After that, the CMCS solution and halloysite nanotubes were mixed into various proportions to form bionanocomposite films. The prepared bionanocomposite films were analyzed based on several characteristics, including water absorption capacity, dressing pH, water vapor transmission rate (WVTR), folding endurance, porosity, thickness, *in vitro* soil degradation, hemolysis, and thrombogenicity. The results indicated that the amount of halloysite nanotubes had a notable impact on the water absorption capacity, folding endurance, thickness, WVTR, and porosity of the bionanocomposite films. Furthermore, these films were found to be non-hemolytic and biodegradable, leading to the conclusion that these bionanocomposite films hold promise for biomedical applications.

**KEYWORDS:** Carboxymethyl-chitosan; Halloysite nanotubes; Bionanocomposite; Wound healing

## I. INTRODUCTION

Polysaccharides have garnered substantial attention recently because of their biocompatibility, biodegradability, and non-toxicity. Among them, Chitosan, a naturally occurring cationic carbohydrate, has been considered a promising candidate due to its remarkable biological properties<sup>1-3</sup>. It is a highly abundant natural polymer, extracted from chitin by treating it with concentrated NaOH, commonly present in exoskeletons of marine creatures such as crabs, shrimps, prawns, lobsters, etc<sup>4, 5</sup>. The water-soluble chitin derivative has found multiple applications in both biomedical and industrial domains<sup>6-10</sup>. However, the low solubility of chitosan in distilled water and conventional solvents limits its applications<sup>11</sup>. So, the chemical modification of chitosan into desired derivatives enhances its properties, making it suitable for various applications. As a result, in this investigation, chitosan is modified into carboxymethyl-chitosan (CMCS). CMCS is an essential water-soluble chitosan derivative that is fruitfully utilized as a biomaterial for research and medical purposes<sup>12, 13</sup>. It has garnered considerable attention from researchers because of its improved properties, including high solubility in water, excellent biocompatibility, and strong biodegradability<sup>14</sup>. Furthermore, it aids the proliferation of skin fibroblasts and encourages neovascularization<sup>15</sup>. Conversely, halloysite nanotubes (HNTs) are natural nanofillers with a chemical structure similar to kaolin<sup>16</sup>. HNTs possess many interesting properties such as good dispersion capacity, a large aspect ratio, ease of availability, and non-toxic nature<sup>17</sup>. HNTs have been employed as nanofillers to increase, not only the thermal stability and mechanical strength, but also other properties of various polymers such as sodium alginate, starch, chitosan, and poly (vinyl alcohol), among others<sup>8-21</sup>. The present study prepared carboxymethyl-chitosan/halloysite nanotubes bionanocomposite films as a wound dressing. The prepared bionanocomposite films were characterized by various physical properties (thickness, water absorption capacity, dressing pH, water vapour transmission rate (WVTR), folding endurance, and porosity) as well as biological properties (*in vitro* blood compatibility, and biodegradability) to investigate their wound healing efficacy.

## II. MATERIALS AND METHODS

### 2.1 Materials

Marine Hydrocolloids, Ernakulum, Cochin, India, chitosan (Ch) with a degree of deacetylation <75%. Halloysite nanotubes were sourced from Sigma-Aldrich. Without any further purification, all chemicals were used just as supplied. Distilled water was employed for all the experiments and sample preparations.

### 2.2 Methods

#### 2.2.1 Synthesis of carboxymethyl-chitosan (CMCS)

CMCS was synthesized following a procedure outlined in previous literature<sup>22</sup>. In brief, 5 g of chitosan was mixed with isopropanol, and then added 40% NaOH (w/v) dropwise to the reaction mixture, and stirred continuously at ambient temperature for 20 minutes. In the next step, 15 g of monochloroacetic acid was dissolved in an equal volume of isopropanol under continuous stirring. The monochloroacetic acid solution was then gradually added to the aforementioned reaction mixture, and the reaction was maintained at ambient temperature while continuously stirring for 24 hours. After that, the solid product was filtered using filter paper and neutralized with 10% acetic acid. The neutralized product was subsequently suspended in an excess of 70% methanol by following filtration or washing with methanol. Finally, the CMCS product was dried at room temperature and stored in a desiccator for future experiments. The formation mechanism of carboxymethyl-chitosan is illustrated in Fig. 1.

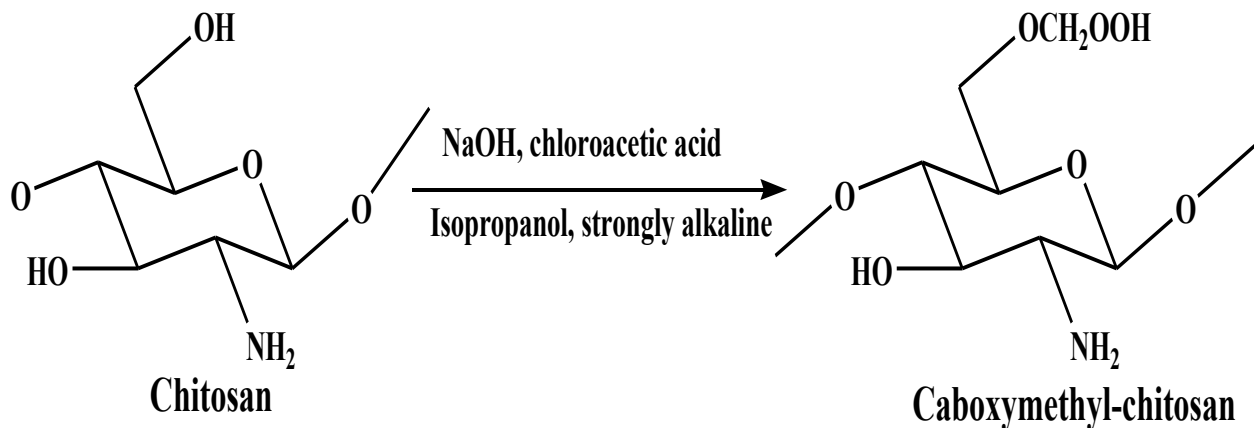


Fig. 1- Synthesis procedure of carboxymethyl-chitosan derivative of chitosan (Adopted from reference 14).

#### 2.2.2 Preparation of CMCS/HNTs bionanocomposite films

CMCS/HNTs bionanocomposite films were fabricated using the solution casting method, with polyethylene glycol as a plasticizer. Briefly, CMCS and HNTs solutions were prepared by dissolving CMCS and HNTs powders separately in distilled water, respectively. Then, the binary solutions were blended in various ratios and stirred continuously to form the binary solution mixture. The binary solution mixture was poured into a polypropylene plate and left in an oven at 37 °C overnight to make the bionanocomposite films. A pure CMCS film, prepared without the halloysite nanotubes and denoted as C0 was shown in Table 1. The C0 film was used as a control throughout the experiment. The thickness of all bionanocomposite films was measured using a screw gauge at five random points on each film and the average thickness was recorded.

#### 2.2.3 Dressing pH

The dressing pH was recorded by dipping each CMCS/HNTs bionanocomposite film and C0 film (25 mm × 25 mm) in a glass beaker containing phosphate buffer solution (pH 7.4) until equilibrium was reached. Afterward, the bionanocomposite film was removed and the digital pH meter was used to record the pH of the remaining solution.

#### 2.2.4 Folding endurance

To calculate the folding endurance, each bionanocomposite film was continuously folded at the same spot up to 300 times<sup>20</sup>. The number of folds achieved without any visible cracks was recorded. The average value was used to measure the folding endurance of the each bionanocomposite film.

### 2.2.5 Moisture Content

Gravimetric analysis was used to determine the moisture content of the CMCS/HNTs bionanocomposite films and C0 films. Each film (WI) was first precisely weighed, and then it was dried for 5 hours at 105 °C in an oven. The drying weight (WD) of each film was further measured. The moisture content was calculated using the equation below

$$\text{Moisture Content} = [WI - WD/WI] \times 100$$

### 2.2.6 Porosity

The porosity of all the prepared CMCS/HNTs bionanocomposite film and C0 film was calculated via the liquid displacement method described in previous studies<sup>23</sup>. In brief, the preweighed films were immersed separately into each beaker containing ethanol till the saturation. The film was taken out of the ethanol and further weighed. This equation was used to figure out the porosity of the film.

$$\% \text{ porosity} = (W2 - W1 - W3 / W2 - W3) \times 100$$

where, W1 denotes the initial known weight of the prepared film, W2 is the combined weight of ethanol and the immersed film, and W3 is the weight of ethanol after the film has been removed.

### 2.2.7 Water absorption capacity

A gravimetric method was used to determine the water absorption capacity of bionanocomposite films. It was placed into a beaker with 15 mL of freshly made 0.9% saline solution (pH 7.4) and kept at 37 °C. Each film had a known weight (WD). At regular intervals, the swollen film (WS) was taken out of the saline solution and immediately weighed on a digital analytical balance. Any excess water on the film surface was gently blotted off with filter paper before weighing. The water absorption capacity (WAC) was calculated via the specified equation.

$$\text{WAC} = [WS - WD/WD] \times 100$$

The experimental data were shown as the mean ± standard deviation (SD) for a sample size of n = 3.

### 2.2.8 Water vapour transmission rate (WVTR)

The WVTR of the prepared films was investigated by adopting a standard method described elsewhere<sup>24</sup>. Briefly, each film was cut in a circular shape and taped to the mouth of a glass beaker filled with 15 mL of distilled water with tape. A glass breaker was kept in an incubator set at 37°C for 24 hours. Water loss through the above-said film was recorded by weighing, and the plot between weight loss and time was generated. The WVTR was determined from the equation below:

$$\text{WVTR (g/m}^2\text{/day)} = M \times 24 / A \cdot T$$

where, **M** indicates mass loss, **T** is time (in hours) during the mass loss, and **A** is the exposed area of film.

### 2.2.9 In vitro blood compatibility

The following methods were used to investigate the prepared bionanocomposite film and control *in vitro* blood compatibility.

#### 2.2.9.1 Hemolysis study

The acid citrate dextrose (ACD) blood used in the hemolysis study, was made by mixing 9 mL of fresh blood with 1 mL of freshly prepared ACD solution<sup>25</sup>. Approximately, 0.544 g of anhydrous citric acid, 1.65 g of trisodium citrate dehydrate, and 1.84 g of dextrose monohydrate were mixed with 75 mL of distilled water to make the ACD solution<sup>26</sup>. A prepared film (1 cm × 1 cm) was put in a falcon tube with 9 mL of normal saline solution and incubated at 37 °C for 30 minutes. Afterward, 1 mL of ACD blood was introduced into the falcon tube. For the negative control, a 1:9 ratio mix of ACD blood and freshly prepared saline solution (pH 7.4) was used. This showed that there was no hemolysis. Conversely, complete hemolysis was achieved with a 1:9 ratio of ACD blood and distilled water. For one hour, the falcon tubes were kept at 37 °C. Each falcon tube was centrifuged at 2000 rpm for 5 minutes<sup>23</sup>. Then, a UV-visible spectrophotometer was used to measure the supernatant's optical density (OD) at 545 nm<sup>27</sup>. All the experiments on

hemolysis were done thrice with each supernatant, and the following equation was used to find the percentage of hemolysis.

$$\text{Hemolysis (\%)} = \frac{[\text{OD}_{\text{test}} - \text{OD}_{\text{neg}} / \text{OD}_{\text{pos}} - \text{OD}_{\text{neg}}] \times 100}{}$$

where,  $\text{OD}_{\text{test}}$ ,  $\text{OD}_{\text{neg}}$ , and  $\text{OD}_{\text{pos}}$  represent the absorbance of test film, negative control, and positive control respectively.

According to 'The American Society for Testing and Materials (ASTM)-F 756-00 method, materials with a hemolysis percentage greater than 5% are classified as hemolytic, those with percentages between 2% and 5% are considered slightly hemolytic, and materials with less than 2% hemolysis are considered as non-hemolytic<sup>28</sup>.

### 2.2.9.2 Thrombogenicity assay

The thrombus formation experiment was performed according to the kinetic method published by Dey and Ray<sup>29</sup>. This was accomplished by applying 0.2 mL of ACD blood to the surface of the prepared film and adding 0.02 mL of 0.1 M calcium chloride solution to start the blood clotting process. Then, 5 mL of distilled water was added to stop the formation of clots after predefined intervals of 15, 30, 45, and 60 minutes. After that the resultant clot was subsequently fixed in 5 mL of 36 % formaldehyde solution. Finally, distilled water was used to wash the fixed clot, filter paper to blot it, and an electronic balance to weigh it.

### 2.2.10 In vitro soil degradation study

The degradation rate of the CMCS/HNTs bionanocomposite films and C0 film was studied by measuring the weight loss for 4 months. The bionanocomposite films were buried in a box filled with soil and retrieved at fixed time intervals. After removal, the films were cleaned with tissue paper, dried, and weighed. All the experiments were conducted in triplicate, and the mean values were used for the calculations.

## III. RESULTS AND DISCUSSION

CMCS/HNTS bionanocomposite films were created using a simple solution casting and evaporation technique. As shown in Table 1, the average thickness of all the bionanocomposite films and control ranged from  $32.50 \pm 1.50$ - $39.75 \pm 0.50 \mu\text{m}$ . The results indicated that the addition of more halloysite nanotubes to the solution mixture increased the thickness of the film. According to the Table 1, the prepared films also had a moisture content of about 6%.

Table 1. Sample code (s) and physical properties of the prepared bionanocomposite films.

Sample code	Carboxymethyl-chitosan (mL)	Halloysite-nanotubes (mL)	Thickness ( $\mu\text{m}$ )	Moisture Content (%)	Dressing pH
C0	3	0	$32.50 \pm 1.50$	$5.77 \pm 0.12$	$6.23 \pm 0.02$
C2H1	2	1	$33.75 \pm 1.00$	$6.15 \pm 0.10$	$6.34 \pm 0.01$
C1H1	1.5	1.5	$35.00 \pm 1.25$	$5.83 \pm 0.10$	$6.41 \pm 0.03$
C1H2	1	2	$39.75 \pm 0.50$	$6.07 \pm 0.08$	$6.52 \pm 0.02$

### 3.1 Dressing pH

Any materials, that are used to help a wound heal should maintain the wound area slightly acidic condition at the wound area. According to previous reports, a dressing material with a slightly acidic pH has a significant effect on the healing process of wounds. The dressing pH of the prepared bionanocomposite films ranged between  $6.23 \pm 0.02$  to  $6.52 \pm 0.02$  as shown in Table 1. The pH values of these bionanocomposite films aligned with the reported pH levels of several commercially available synthetics wound care products, such as Algoplaque ( $5.8 \pm 0.08$ ), Askina Biofilm Transparent ( $6.0 \pm 0.04$ ), Comfeel Plus Transparent ( $6.4 \pm 0.05$ ), Comfeel Plus Flexible ( $6.6 \pm 0.06$ ), and Askina Transorbent ( $7.0 \pm 0.04$ )<sup>20, 30</sup>. Therefore, it was concluded that the above-mentioned films were quite good as wound dressing in terms of dressing pH.

### 3.2 Folding endurance

The results indicated that the bionanocomposite films were more folding-resistant when halloysite nanotubes were incorporated into the CMCS solution. As shown in Fig. 3, the C1H1 bionanocomposite film shows a maximum folding endurance than the control or any other prepared bionanocomposite films. This is due to the reinforcing nature of halloysite nanotubes. The prepared bionanocomposite films showed good flexibility and strength since their folding endurance values of the prepared films were determined to be optimal.

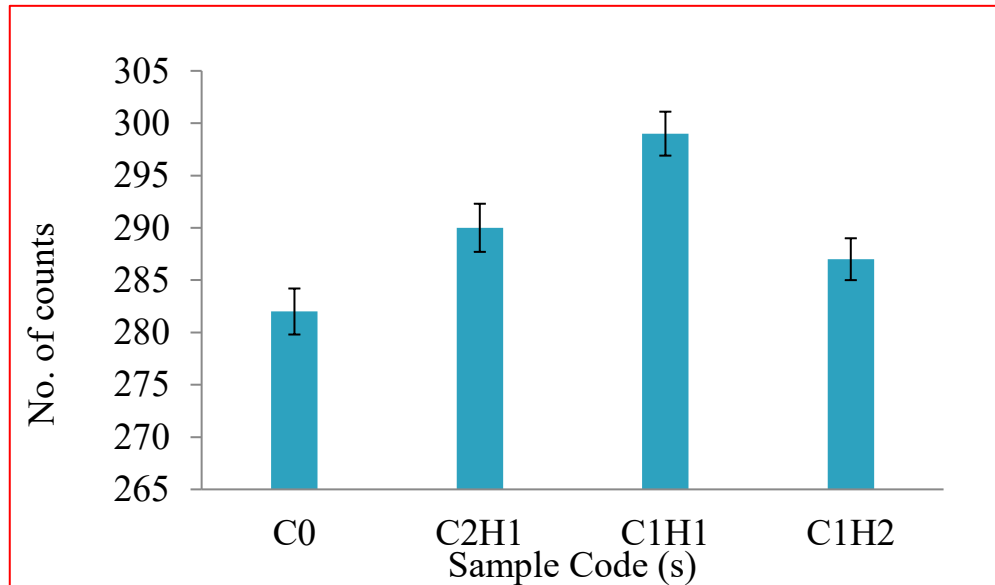


Fig. 3- Folding endurance of the prepared bionanocomposite films including control (C0)

### 3.3 Porosity

Using the liquid displacement, the porosity of the prepared bionanocomposite films was examined. The porosity of all films, including the control, ranged from  $66.89 \pm 0.3$  to  $79.25 \pm 0.4\%$ , as illustrated in Fig. 4. According to the findings, the porosity of bionanocomposite films reduced as the halloysite nanotubes content increased. This observation aligns with previously published findings on the porosity of chitosan/starch films containing halloysite nanotubes by Devi and Dutta<sup>20</sup>. In addition, Kumar et al.<sup>31</sup> reported that the porous dressing materials are beneficial for absorbing excess wound exudates and make it easier for cells to receive nutrients and oxygen<sup>32</sup>.

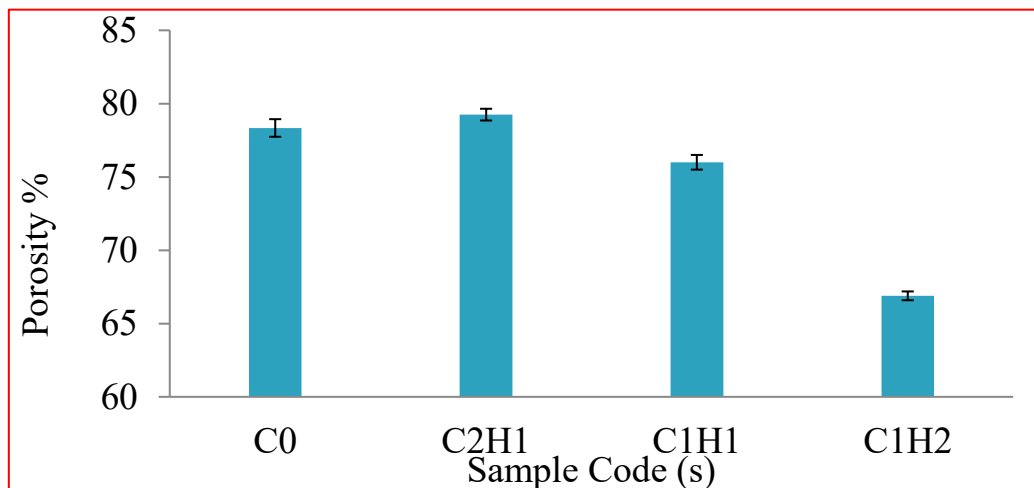


Fig. 4- Porosity of the prepared bionanocomposite films including control (C0).

### 3.4 Water absorption capacity

The water absorption capacity of any dressing plays crucial role in wound healing system by absorbing large wound exudates, maintaining moist environment, and preventing bacterial infection. The prepared bionanocomposite films' water absorption capacities were shown in Fig. 5. As demonstrated in Fig. 5, the incorporation of HNTs significantly boosts the water absorption capacity of the said bionanocomposite films, with the C1H2 film showing the most significant improvements. The higher water absorption capacity of these films is attributed to the hydrophilic nature of HNTs, which aligns with the findings reported by Devi and Dutta<sup>20</sup>. They revealed that the increasing content of halloysite nanotube in chitosan/starch/halloysite nanocomposites raised their water absorption capacity.

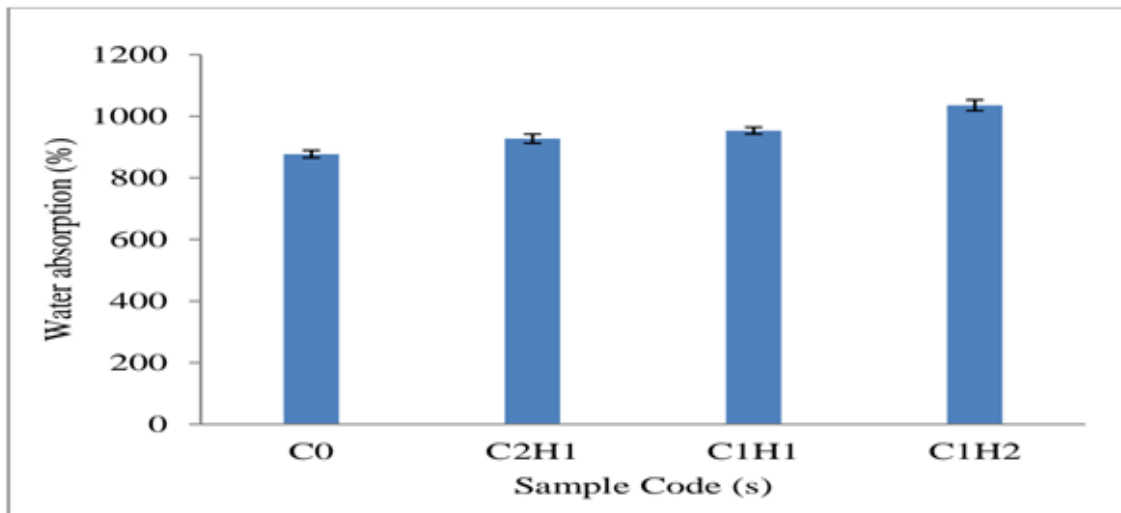


Fig. 5- Water absorption capacity of all the prepared bionanocomposite films.

### 3.5 Water vapour transmission rate (WVTR)

According to Queen et al.<sup>33</sup>, a WVTR of 2000–2500 g/m<sup>2</sup>/day is optimal for maintaining proper moisture levels, preventing severe dehydration, and absorbing extra exudate at the wound surface. The higher WVTR value can dry the wounds faster and may cause scarring, whereas the lower WVTR could result in the accumulation of wound fluids, slowing the healing process and raising the risk of microbial infection<sup>20, 23, 34</sup>. The WVTR of the prepared bionanocomposite films was checked, and results were depicted in Fig. 6. The prepared films had WVTR values ranging from 1960±2.89 to 2098±2.63 g<sup>-2</sup> day<sup>-1</sup>, similar to the ideal range for wound care products reported by Queen et al.<sup>33</sup>

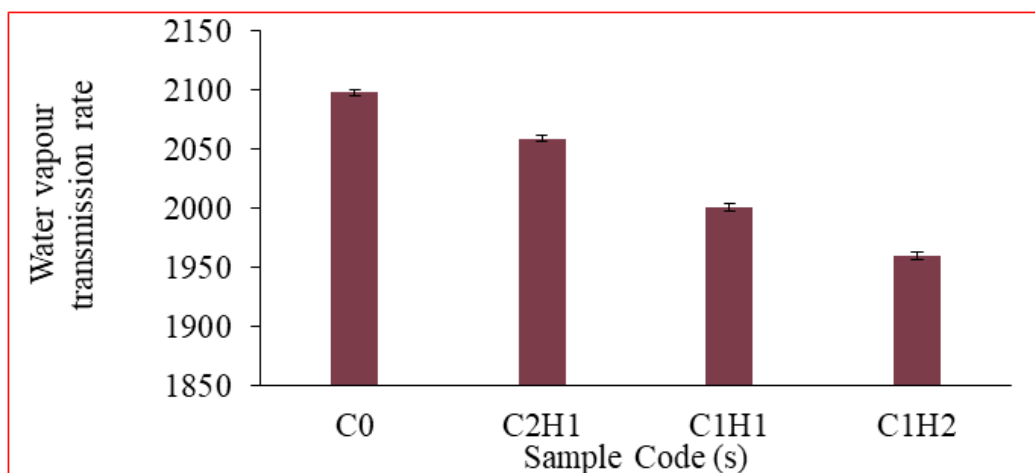


Fig. 6- WVTR of the prepared bionanocomposite films including control (C0).

### 3.6 Hemolysis study

The hemolysis experiment was performed on the surfaces of the prepared bionanocomposite films and the control. According to the ASTM F 756-00 method<sup>28</sup>, a substance is considered non-hemolytic, if its hemolysis value is less than 2%. The prepared bionanocomposite films and pure CMCS film had hemolysis values of 1.25±0.02-1.88±0.02 %, as shown in Fig. 7. The results showed that all prepared films' hemolysis values were less than 2%. This clearly indicated that the bionanocomposite films and the control were non-hemolytic in nature.

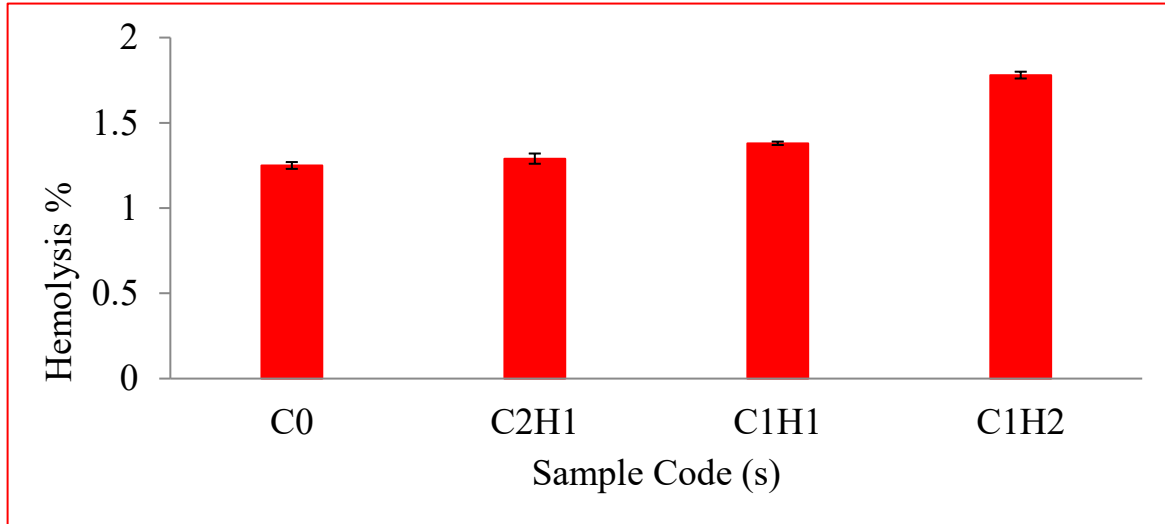


Fig. 7- Hemolysis study of the prepared bionanocomposite films including control (C0).

### 3.7 Thrombogenicity assay

The weight of blood clot formation was recorded for each film at regular intervals and the results are presented in Table 2. Table 2 shows that the weight of blood clot formation decreases with increasing contact time of blood with the tested films. According to the literature, the surface properties have a major molecular impact on surface-induced thrombosis. The inhibition of blood clotting properties by the prepared films could be attributed to an adverse interaction of blood components via protein denaturation<sup>29</sup>. A group of researchers also reported that the increased hydrophilicity has no direct effect on blood compatibility<sup>35</sup>.

Table 2- Thrombogenicity assay of the prepared bionanocomposite films including control (C0).

Sample Code	Weight of clot (g)			
	15 min	30 min	45 min	60 min
C0	0.214	0.189	0.104	0.086
C2H1	0.287	0.173	0.099	0.079
C1H1	0.302	0.191	0.120	0.081
C1H2	0.298	0.165	0.101	0.068

### 3.8 In vitro soil degradation study

The weight loss percentages of the prepared films were 63%, 52%, 49%, and 46.50% for C0 (control), C2H1, C1H1,



and C1H2 after 4 months. The findings indicated that the weight loss % of the bionanocomposite films decreased with an increase in the quantity of HNTs in the CMCS solution increased. This trend aligns with the findings of Liu et al.<sup>36</sup>, who also observed that the degradation rate of the composite sponges slowed down as the weight % of HNTs increased. Further, the result also indicated that C2H1 bionanocomposite film showed the highest weight loss percentage i.e. 52% (except control). This is due to the presence of a hydrophilic nature and the high quantity of carboxymethyl-chitosan in C2H1 film. This study proves that the prepared films would be decomposed in a few months once discarded, and eventually would not harm nature.

#### IV. CONCLUSION

Bionanocomposite films were prepared using carboxymethyl-chitosan (CMCS) and halloysite nanotubes (HNTs) via the solution casting technique. The prepared bionanocomposite films were characterized by various physico-biological properties. The result showed that the incorporation of HNTs into the CMCS solution not only enhanced the mechanical strength, as indicated by increased folding endurance but also boosted the water absorption capacity and water vapor transmission rate (WVTR). The pH of the dressing for all the prepared films was recorded, and it was in the acceptable range of the ideal value for any wound dressings. Further, the films were confirmed to be non-hemolytic in nature. *In vitro* soil degradation tests showed that the films completely degraded after a certain time, demonstrating their potential for environmental biodegradability. Therefore, the prepared bionanocomposite films might be potentially utilized for wound dressing applications.

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#### REFERENCES

1. R.C.F. Cheung, T.B. Ng, J.K. Wong, and W.Y. Chan, "Chitosan: an update on potential biomedical and pharmaceutical applications", *Mar Drugs*, vol. 13, pp.5156-5186, 2015.
2. I. Bano, M. Arshad, T. Yasin, M.A. Ghauri, and M. Younus, "Chitosan: a potential biopolymer for wound management", *Int J Biol Macromol*, vol. 102, pp. 380-383, 2017.
3. S. Mania, R. Tylingo, E. Augustin, K. Guwca, J. Szwacki, and H. Staroszczyk, "Investigation of an elutable N-propylphosphonic acid chitosan derivative composition with a chitosan matrix prepared from carbonic acid solution", *Carbohydr Polym*, vol. 179, pp. 196-206, 2018
4. W. Wang, Q. Meng, Q. Li, J. Liu, M. Zhou, Z. Jin, and K. Zhao, "Chitosan derivatives and their application in biomedicine", *Int J Mol Sci*, vol. 21, pp. 487, 2020.
5. N. Devi, and J. Dutta, "A mini review on chitin/chitosan based wound dressings from shrimps and crabs sources", *Asian Chitin J*, vol. 11, pp. 1-6, 2015.
6. E. Szymanska, and K. Winnicka, Stability of chitosan- a challenge for pharmaceutical and biomedical applications", *Mar Drugs*, vol. 13, pp. 1819-1846, 2015.
7. A. J. Al-Manhel, A.R.S. Al-Hilphy, and A.K. Niamah, "Extraction of chitosan, 212haracterization and its use for water purification", *J Saudi Soc Agric Sci.*, vol, 17, pp. 186-190, 2018
8. S. Samadieh, and M. Sadri, "Preparation and biomedical properties of transparent chitosan/gelatin/honey/aloe vera nanocomposite", *Nanomed Res J.*, vol. 5, pp. 1-12, 2020.
9. N. Boudouaia, Z. Bengharez, and S. Jellali, "Preparation and characterization of chitosan extracted from shrimp shells waste and chitosan film: application for Eriochrome black T removal from aqueous solutions", *Appl Water Sci.*, vol. 9, pp. 91,2019.
10. R. Onnainty, and G. Granero, "Chitosan-clay based nanocomposites; Promising materials for drug delivery applications", *Nanomed Nanotechnol J.*, vol. 1, pp. 114, 2014
11. J. Li, C. Cai, J. Li, J. Li, T. Sun, L. Wang, H. Wu, and G. Yu G, "Chitosan-based nanomaterials for drug delivery", *Molecules*, vol. 23, pp. 2661, 2018.
12. Y. Cheng, Z. Hu, Y. Zhao, Z. Zou, S. Lu, B. Zhang, and S. Li, " Sponges of carboxymethyl chitosan grafted with collagen peptides for wound healing", *Int J Mol Sci.*, vol. 20, pp. 3890, 2019.
13. T. Sun, B. Zhan, W. Zhang, D. Qin, G. Xia, H. Zhang, M. Peng, S.A. Li, Y. Zhang, Y. Gao, and W.H. Lee, Carboxymethyl chitosan nanoparticles loaded with bioactive peptide OH-CATH30 benefit nonscar wound

- healing” International Journal of Nanomedicine, vol. 13, pp. 5771, 2018.
14. L. Upadhyaya, J. Singh, V. Agarwal, and R.P. Tewari, “Biomedical applications of carboxymethyl chitosans”, Carbohydr Polym., vol. 91, pp. 452-466, 2013.
  15. X. Huang, Y. Zhang, X. Zhang, Xu, X. Chen, and S. Wei, “Influence of radiation crosslinked carboxymethyl-chitosan/gelatin hydrogel on cutaneous wound healing”, Mater Sci Eng. C., vol. 33: pp. 4816-4826, 2013.
  16. M. Liu, Y. Zhang, C. Wu, S. Xiong, and C. Zhou, “Chitosan/halloysite nanotubes bionanocomposites: Structure, mechanical properties and biocompatibility”, Int J Biol Macromol., vol. 51, pp. 566-575, 2012
  17. M. Du, B. Guo, and D. Jia, “Newly emerging applications of halloysite nanotubes: a review”, Polym Int., vol. 59, pp. 574-582, 2010.
  18. B. Huang, M. Liu, Z. Long, Y. Shen, and C. Zhou, “Effects of halloysite nanotubes on physical properties and cytocompatibility of alginate composite hydrogels”, Mater Sci Eng C., vol. 70, pp. 303-310, 2017.
  19. R.T. De Silva, P. Pasbakhsh, K.L. Goh, S-P. Chai, and H. Ismail, “Physico-chemical characterization of chitosan/halloysite composite membranes” Polym Test., vol. 32, pp. 265-271, 2013.
  20. N. Devi, and J. Dutta, “Development and in vitro characterization of chitosan/starch/halloysite nanotubes ternary nanocomposite films”, Int J Biol Macromol., vol. 127, pp. 222-231, 2019.
  21. Z.W. Abdullah, and Y. Dong, “Correction to: Preparation and characterization of poly(vinyl) alcohol (PVA)/starch (ST)/halloysite nanotube (HNT) nanocomposite films as renewable materials”, Journal of Material Science, vol. 53, pp. 3455, 2017.
  22. Farag RK, Mohamed RR. Synthesis and characterization of carboxymethyl Chitosan nanogels for swelling studies and antimicrobial activity. Molecules. 2013; 18: 190-203.
  23. Devi N, Dutta J. Preparation and characterization of chitosan-bentonite nanocomposite films for wound healing application. Int J Biol Macromol. 2017; 104: 1897-1904.
  24. P.Wu, A.C. Fisher, P.P. Foo, D. Queen, J.D.S. Gaylor, “In vitro assessment of water vapour transmission of synthetic wound dressings”, Biomaterials, vol. 16, pp. 171-175, 1995.
  25. E.A. Kamoun, E.R.S. Kenway, K.T.M. Tamer, M.A. El-Meligy, and M.S.M. Eldin, “Poly (vinyl alcohol)- alginate physically crosslinked hydrogel membranes for wound dressing applications: Characterization and bio-evaluation”, Arabian Journal of Chemistry, vol. 8, pp. 38-47, 2015.
  26. D. Archana, B.K. Singh, J. Dutta, and P. K. Dutta, “Chitosan-PVP-nano silver oxide wound dressing: In vitro and in vivo evaluation”, International Journal of Biological Macromolecule, vol. 73, pp. 49-57, 2015.
  27. A. Chhatri, J. Bajpai, A.K. Bajpai, S.S. Sandhu, N. Jain, and J. Biswas, “Cryogenic fabrication of savlon loaded macroporous blends of alginate and polyvinyl alcohol (PVA). Swelling, deswelling and antibacterial behaviors”, Carbohydr Polym., vol. 83, pp. 876-882, 2011.
  28. American society for testing and materials: Standard practice for assessment of haemolytic properties of materials, 2000. ASTM F 756-00, Philadelphia.
  29. R.K. Dey, and A.R. Ray, “Synthesis, characterization, and blood compatibility of polyamidoamines copolymers”, Biomaterials, vol. 24, pp. 2985-2993, 2003.
  30. <http://www.worldwidewounds.com/1997/july/Thomas-Hydronet/hydronet.html>
  31. P.T.S. Kumar, V.K. Lakshmanan, R. Biswas, S.V. Nair, and R. Jayakumar, “Synthesis and Biological Evaluation of Chitin Hydrogel/Nano ZnO Composite Bandage as Antibacterial Wound Dressing”, J Biomed Nanotechnol, vol. 8, pp. 891-900, 2012.
  32. R. Jayakumar, M. Prabaharan, P.T.S. Kumar, S.V. Nair, and H. Tamura H, “Biomaterials based on chitin and chitosan in wound dressing applications”, Biotech Adv, vol. 29, pp. 322-327, 2011.
  33. D. Queen, J.D.S. Gaylor, J.H. Evans, J.M. Courtney, and W.H. Reid, “The preclinical evaluation of the water vapour transmission rate through burn wound dressings”, Biomaterials, vol. 8, pp. 367-371, 1987.
  34. R. Poonguzhali, S.K. Basha, and V.S. Kumari, “Synthesis and characterization of chitosan/poly (vinylpyrrolidone) biocomposite for biomedical application”, Polymer Bulletin, vol. 74, 2185-2201, 2017.
  35. K. Ishihara, Y. Iwasaki, S. Ebihara, Y. Shindo, and Nakabayashi, “Photoinduced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on polyethylene membrane surface for obtaining blood cell adhesion resistance”, Col Surf B Bioint, vol. 18, pp. 325-335, 2000
  36. M. Liu, Y. Shen, P. Ao, L. Dai, Z. Liu, C. Zhou, “The improvement of hemostatic and wound healing property of chitosan by halloysite nanotubes”, RSC Adv., vol. 4, pp. 23540-22553, 2014



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