A REVIEW ON MECHANICAL PROPERTIES OF CHITOSAN-BASED FOR WOUND DRESSING MATERIALS

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Abstract

An effective wound dressing material should be flexible structure, biocompatible, maintain wound moisture and adsorb exudate. The rate of the wound healing process depends on the type of wound care dressing materials. The chitosan-based dressing has become attention for wound dressing application for decades. This study aims to review the mechanical characterization of chitosan-based material for wound healing applications. In this review, the process of searching research papers was performed according to the PRISMA-P protocol that begins by searching literature on the selected databases such as Science Direct, PubMed, and Google Scholar from the year of 2012 to 2022. The pre-determined keywords (chitosan-based material, physicochemical characterization, wound dressing, wound healing, wound treatment) were used in data searching protocol. The search retrieved 284 articles. Assessment of eligibility retrieved 19 articles based on the inclusion and exclusion criteria. This review provides the knowledge of physicochemical characterization studied on chitosan-based wound dressing material including the porosity, swelling behaviour, water vapour transmission rate and mechanical properties.

Keywords: Chitosan-Based Material, Physicochemical Characterization, Wound Dressing, Wound Healing, Wound Treatment

Introduction

Wound dressings are essential medical equipment that plays a significant role in the healing process. An effective wound dressing must maintain moisture and humidity, provide protection against bacterial infection, increase the growth factor activity, be permeable to the gas exchange between the wound and dressing, absorb wound exudate, and promote healing (1). Hydrogels, hydrocolloids, alginates, foams, and films are the types of wound dressing that are frequently used in medical practice (2). Different types of wound dressing and material selection would impact the healing rate capability. A promising material for wound healing applications is biocompatible, absorbable polymers like chitosan.

Chitosan is linear-chain polysaccharides originate from chitin's deacetylation which exhibits antibacterial, biocompatible, and biodegradable properties (3). Chitosan has shown promising properties in hastening wound healing by activating fibroblasts, inflammatory cells and macrophages, thereby enhancing the inflammatory stage. Thus, the inflammatory stage can be minimised, and initiated the proliferative stage earlier which contributes to the wound healing process (4). Furthermore, its physical and biological features can be modified to satisfy the targeted wound healing applications such as films, sponges, scaffolds, nanoparticles, and hydrogels.

This review focused on the mechanical properties reported from chitosan-based dressing material that has been widely studied for wound healing applications. Understanding on this aspect associated with wound healing mechanisms that crucial in producing efficient wound dressing products.

Materials and Methods

Search Strategy

The manuscripts between 2012 till 2022 were retrieved in the following databases: Science Direct, PubMed, and engine Google Scholar using PRISMA-P protocol. A Boolean Strategy was applied in this method. To increase the scope of the search results, the predetermined keywords (physicochemical characterisation, chitosan-based material, wound dressing, wound healing, wound treatment) were utilized and combined with the Boolean Operator 'AND' or 'OR'. In order to find the reliable articles from the electronic journal databases, the titles and abstracts of potential articles were separately screened. Furthermore, a non-automated manual search was performed to carefully check the bibliographies of the chosen publications in order to find any additional relevant potential articles. Each step was carefully processed to ensure feasibility, transparency and replicability to reanalyse. To eliminate duplication of work, Microsoft Excel was used to compile all titles and references of articles. Next, Mendeley was used as a reference manager to merge the findings of the selected studies.

Study Selection

Research articles focusing mainly on physicochemical characterisation, chitosan material, and wound dressing within the past ten years (2012 till 2022) were selected to narrow the review. The articles were selected and further categorised according to the types of the chitosan wound dressing and their characterisation (for example, SEM, swelling properties, and mechanical strength). Studies involving the usage of other material and those blacklisted journals were excluded.

Data Extraction and Analysis

The articles were extensively evaluated the inclusion criteria and quality of the articles to ensure the eligibility. The data on physicochemical characterisation of chitosan-based materials for wound healing applications were independently extracted. The physicochemical characterisations such as SEM, swelling properties, and mechanical strength were included and compiled in a Table 1 and Table 2. The reference citations were exported to the reference manager software which is Mendeley. To determine the study's strength, the data gathered from the research were sorted, concluded, and compared.

Results

A total of 284 research publications were found using the Google Scholar search engine, Science Direct, and PubMed indexes. After applying inclusion and exclusion criteria, we retrieved 19 research articles that discussed the physicochemical characterisation of chitosan-based material (Figure 1). Present studies on the physiochemical characterisation of the chitosan-based material for wound healing are tabulated in Table 1. The author has retrieved studies that have fabricated chitosan-based material into film, hydrogel, foam, scaffold, crosslinked, mat, patch, membrane, and fibre. The extracted papers presented in Table 1 and Table 2 have fabricated chitosan with other components such as silver nanoparticles, polyvinyl pyrrolidone (PVP), hypericum perforatum, nanostarch, honey, gelatine, nanofibrin, maleic anhydride, nanocellulose, Bella Striata, Henna, graphene oxide, cinnamaldehyde and pectin. Each material incorporated with chitosan has given the different impact on the improvement of the wound dressing applications.

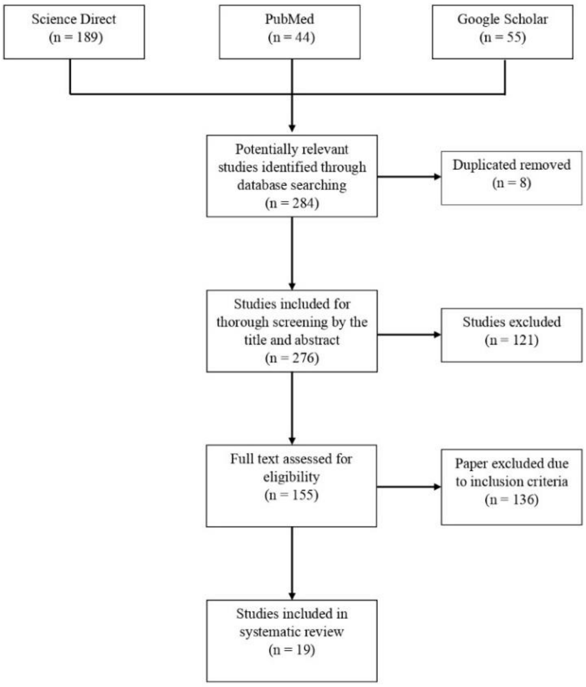

Figure 1: Flow chart showing search, study selection and data extraction strategy.

Table 1: Mechanical properties of chitosan-based dressing sheet/films/maths

Types	Properties	Reference
Ch-SG-AgNP film	SEM: Porous and rough surface Tensile strength: 10.21 ± 0.78 MPa Swelling behaviour: Maximum 185% water absorbing capacity	Marie Arockianathan et al., 2012
Chitosan-PVP-nano silver oxide film	SEM: silver oxide nanoparticles homogeneous distribution Swelling behaviour: After 7 h decrease in swelling observed due to solubility of PVP in water. WVTR: 2000-2150 g^{-2} day^{-1} (ideal value for wound dressing material). Mechanical properties: The tensile strength of CPS film with silver nanoparticle increased to 35.98 ± 0.98 Mpa.	Archana et al., 2015
Chitosan/ H.perforatum film	SEM: Pure chitosan film had smooth surface, the addition of hypericum oil increased roughness and opaqueness of the films. Swelling behaviour: The swelling degrees decreased as the oil content increase. WTVR: The WTVR increased by adding Hypericum perforatum oil to the films. Mechanical properties: The addition of H. perforatum oil reduced the tensile strength.	Güneş & Tıhmınlıoğlu, 2017
CPNS films	SEM: scaffolds pore size was 150-250 µm Swelling behaviour: hydrophilic surface with swelling range of 350-300%. WVTR: scaffolds range of 2539-2205 g/(m^2h) Mechanical properties: The tensile strength decreased from 38-28% with the addition of 3% nanostarch. The elongation at break increased from 35-60%.	Poonguzhali et al., 2018
Chitosan-honey-gelatine hydrogel sheet	SEM: The hydrogel sheets with 40% water content exhibited a smooth surface without the presence of pores. The hydrogel sheet with 130% water exhibited microporous cross-section. The hydrogel sheets with 200% water have porous cross-section with the reduction of pore number but the pore size increased. Swelling behaviour: The equilibrium swelling in water of hydrogel sheets increases as the honey content decreases Mechanical properties: lowest modulus due to the presence of honey.	Wang et al., 2012
Chitosan hydrogel/ nanofibrin bandages	SEM: interconnected porous structure with 200-300 µm size Swelling behaviour: 10-15% degree Mechanical properties: The elongation range was between 40-60% at breakpoints. Tensile strength between 0.02-0.04 Mpa	Kumar et al., 2013
Chitosan/ PEG-MA hydrogels	SEM: interconnected pores structure with 8-20 µm size Swelling behaviour: 230 to 287% swelling degree Mechanical properties: tensile strength between 16.86-34.35 Mpa	Jafari et al., 2019
Henna extracts incorporated in chitosan nanofibrous mats	SEM: The nanofibrous mats containing 0-2 wt% henna extract exhibited the porosity 81, 86 and 91%. Sweeling behaviour: The nanofibrous mats showed 93% swelling degree. Mechanical properties: The tensile modulus decreased from 57.4 to 41.7 Mpa after the incorporation of Henna extract.	Yousefi et al., 2017
Cs/PVA/ GO/CuO patch	SEM: The NC was evenly distributed in the polymeric patch. It shows slight roughness on the surface of the patch. Swelling behaviour: The swelling properties can be seen after day 3, 4 and 5. WVTR: The WVTR of the patch is between 1996-2148 m^{-2} day^{-1}. Mechanical strength: The tensile strength of the patch is 37.84 MPa.	Venkataprasanna et al., 2020

Gelatine/ chitosan/ cinnamaldehyde membranes	SEM: The roughness of membranes surface increased as cinnamaldehyde content increased. Swelling behaviour: The tensile strength decreases as the cinnamaldehyde content increased.	Kenawy et al., 2019

Table 2: Mechanical properties of chitosan-based dressing foams/scaffolds

Types	Properties	Reference
N-carboxymethyl chitosan foams (CMC) 5-methyl pyrrolidinone chitosan foams (MPC) N-succinyl chitosan foams (SC)	SEM: CMC exhibits a larger honeycomb-like porous structure while MPC and SC presented an interlaced fibre-like pattern. Thinner fibre structure observed in SC. Swelling behaviour: SC has the fastest swelling rate. WTVR: SC exhibits the largest hydrophilicity in which it adsorbed larger water vapor.	Moura et al., 2014
Chitosan-collagen-gelatine scaffolds	SEM: Increasing the genipin concentration from 0.5-2.0%, the pore cross-sectional area increased by 180 and 1100 µm^2. Swelling behaviour: The increasing genipin concentration reduced swelling capacity to the scaffold. WVTR: WVTR at 400 g/m^2. Mechanical properties: The compressive stress of scaffold with the increasing genipin concentration were in between 12.11 kPa to 29.17 kPa.	Gorczyca et al., 2014
Collagen-chitosan sponge scaffold encapsulated with thymosin beta 4	SEM: The 50/50 collagen-chitosan scaffolds had a highly interconnected, homogeneous porous structure, and the pore size ranging 110 to 140 µm. Swelling behaviour: The scaffolds were still morphologically stable after 12 days. Mechanical properties: The tensile strength of 50/50 scaffolds were smaller compared to others.	Ti et al., 2015
Gelatine-carboxymethyl chitosan scaffolds	SEM: The pore size of the scaffolds was in between 100 and 200 µm. Mechanical properties: The tensile strength was in range of 0.908 to 0.513 MPa and the value of percentage elongation was between 9.5 to 26.895%. Swelling behaviour: The scaffold with ratio 1:3 of chitosan to gelatine showed maximum swelling index 10.05 at the end of 72 h of analysis.	Agarwal et al., 2016
Spherical nanocellulose (s-NC) reinforced carboxymethyl chitosan scaffolds	SEM: The scaffolds were highly porous with interconnected morphological structure. Swelling behaviour: The scaffolds showed lower swelling efficiency.	Patel et al., 2022
Chitosan crosslinked genipin with oxidised Bletilla striata (CSGB)	SEM: The average pore size is between 201-161 µm. Swelling behaviour: The water retention values were increased with the addition of PO-BSP but as the PO-BSP was 0.5% the water retention ability decrease. Mechanical properties: The addition of PO-BSP cause the tensile strength higher.	Ding et al., 2017

Discussion

The mechanical characteristics of an excellent wound dressing material plays crucial role in enhancing the wound healing rate. An effective wound dressing must have certain features such as the ability to control the moisture, allow gaseous exchange, effectively remove exudates, can be quickly changed and removed, have mechanical strength for wound protection, biocompatible, biodegradable, and elastic (5). These properties can be determined by observing the wound dressings' physicochemical characteristics. Scanning electron microscopy (SEM), swelling properties, mechanical strength, and water vapour transmission rate (WVTR) can be used as an indicator to determine these properties.

Scanning electron microscopy (SEM)

Scanning electron microscopy is an instrument to determine the surface morphology of the material. It uses electrons for imaging, in a similar principle to light microscopes. SEM analysis provides information such as pore shape, size, fillers in the nanocomposite, membrane thickness and as well as the distribution of nanoparticles (6). Most of the studies, used SEM to determine the porosity and distribution of the nanoparticles on their samples. Porosity is one of the crucial parameters for an ideal wound dressing. A proper porosity size enables oxygen to permeate and diffuse from the air to the skin, which is an efficient approach to fasten the process of wound healing (7). However, different forms of wound dressing, such as foams, films, and others, require a different size of porosity to enhance their usability as the wound healing accelerator.

A pure chitosan film was found to have a smooth surface as observed under SEM. Structure porosity of chitosan dressing material varies depending on crosslinker substituent. Study by Marie Arockianathan et al. in 2012, reported on the fabrication of Ch-SG-AgNP that exhibited a porous, and rough surface films (8) with the incorporated nanoparticles. Followed in 2017, Güneş & Tıhmınlıoğlu studied the fabricated a porous chitosan film with the addition of oil. Indeed, the incorporation of H. perforatum oil was found to increase the porosity of the film. The increasing porosity of the film was reported to be affected by the increasing crosslinking interactions between chitosan and the oil (9). This porosity structure could contribute to efficient absorbing properties of wound exudates and oxygen exchange to wound surface (10).

Swelling behaviour

Swelling behaviour analysis is to study the ability of the wound dressing to sustain a moist environment when applied to an open wound surface. The higher the swelling capacity, means the better the moist absorbent of the wound dressing. The behaviour is affected by the hydrophilicity of the material. If it is hydrophilic, higher the swelling property due to improved water binding ability and a stronger affinity for water molecules (11). The swelling behaviour is crucial to indicate the absorption of exudates for wound healing materials as it keeps the wound dry and prevents airborne infection (12). The study of swelling behaviour of the wound dressing material had been implemented by some researchers. It was found that most of the chitosan-based wound dressing showed a good swelling behaviour, however the materials added into chitosan introduce different level of swelling behaviour properties. Jafari et al. had mentioned the increase in the PEG-MA/CS ratio from 1.3:1 to 2:1 exhibited a reduced in the percentage of swelling, yet the ratio 3:1 of PEG-MA/CS showed maximum swelling percentage. The first occurence is affected by the crosslinking density as there are more linkages between the polymer's backbone and crosslinker, the mobility of the polymer chain is severely constrained, which lowers water uptake. The second phenomena was believed to be affected by the increasing water binding ability toward water molecules (11). In addition, the hydrophobic nature of the incorporated material can reduces the water absorption of the dressing.

Water vapour transmission rate

Water vapour transmission rate (WVTR) is a measure of the transmission of water vapour through a substance. In short, WVTR is a water vapour barrier permeability measure. The WVTR is an essential parameter for an ideal wound dressing as it controls the wound healing, granulation of tissue growth, and the reepithelialisation of skin (13). The optimum range of WVTR is between 2000-2500 m-2 day-1 to prevent dehydration of wound and provide adequate humidity for the healing process (14). Besides, the faster the WVTR, the slower the healing mechanism. From the observation, water vapour transmission rate was affected the by the porosity of the material. The higher the amount of porosity in the materials, the greater the WVTR. The hypothesis is proven by the Güneş & Tıhmınlıoğlu, in 2017, they produced chitosan/H. perforatum films and found out that the WVTR increase after the incorporation of oil. The oil affects the surface morphology of the sample in which it forms more pore on the chitosan film. It was also reported that, if the WVTR is larger than the optimum range, the WVTR would dry the wound quickly and produces scar. In addition, the hydrophilicity of the wound dressing material may impact the WVTR. The synthesis of Cs/PVA patch exhibited optimum range of WVTR as a result of the lower crystallinity of CS and PVA and hydrophilic nature, however, the fabrication of Cs/PVA/GO/CuO results in lower WVTR due to the addition of the GO/CuO NP that clogged the Cs/PVA pores (14). In short, the addition of substituent materials into chitosan wound dressing affects the WVTR.

Other Mechanical properties

The study of mechanical properties is to assess the difficulty of handling the wound dressing. For example, the poor mechanical strength of hydrogels makes them difficult to handle. Furthermore, a wound dressing is essential to be strong and flexible that able to cover the wound surface during the recovery process. Mechanical strength can be determined by measuring the tensile strength of the wound dressing. The incorporation of other materials into the wound dressing may impact the mechanical properties due to the establishment of crosslinking, hydrogen bonding, or the distribution of the nanoparticles, however, it depends on the types of the materials that are incorporated into the wound dressings.

The incorporation of additional material into the wound dressing significantly impacts the tensile strength. The chitosan itself is a brittle polymer with poor mechanical properties. The addition of nanoparticle may increase the tensile strength. At first, the incorporation of PEG-MA to chitosan reduces the tensile strength as the high concentration of PEG-MA behave as plasticiser in hydrogels but the incorporation of TiO2 nanoparticles improved the strength of the tensile due to the twisted polymer (11). Venkataprasanna et al. in 2020, had fabricated Cs/PVA and Cs/PVA/GO/CuO patches. It was found that the strength of tensile of the latter patch has higher tensile strength because of the formation of hydrogen bond between the nanocomposite of GO/CuO. Besides, the tensile strength is increased by the nanocomposite's homogeneous distribution.

Conclusion

The mechanical properties such as the porosity characterised by SEM, swelling behaviour, water vapour transmission rate and other mechanical properties that affect the wound dressing efficiency. It was found that the incorporation of other substituent material could significantly add value of the chitosan-based dressing material’s performance. Knowledge from this work might help in the development of ideal chitosan-based dressing material for targeted wound healing application.

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Competing interests

The authors declare that they have no competing interests.

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