ROYAL ACADEMY OF ENGINEERING

Newton – Al-Farabi Partnership Programme

Industry Academia Partnership Program
Newton-Al-Farabi Partnership Programme
Al-Farabi Kazakh National University
University of Reading

PROCEEDINGS

of the workshop

"POLYMERS AND HYDROGELS FOR WOUND CARE AND OTHER BIOMEDICAL APPLICATIONS"

Workshop on Industry Academia Partnership Program collaboration with Kazakhstan in the frame of project

"DEVELOPING RADIATION TECHNOLOGY FOR MANUFACTURING HYDROGEL WOUND DRESSINGS WITH ANTIMICROBIAL ACTIVITY"

12-13 April 2017

in Al-Farabi Kazakh National University, Almaty, Kazakhstan

Almaty 2017

Contents

Developing radiation technology for manufacturing hydrogel wound dressings with antimicrobial activity

[1]Zh.A. Nurpeissova, [1]A.M. Tumabayeva, [1]G.K. Abilova, [2]Zh.I. Beksultanov, [1]G.S. Irmukhametova, [3]V.V. Khutoryanskiy
[1]al-Farabi Kazakh National University, Almaty, Kazakhstan
[2]Institute of Nuclear Physics, Almaty, Kazakhstan
[3]University of Reading, Reading, UK
e-mail: galiya.irmukhametova@kaznu.kz

Chronic wounds are a serious medical condition that takes a minimum of eight weeks up to many years to heal. They can seriously affect the quality of life of patients and may lead to mobility limitations and depression. The majority of commercial hydrogel wound dressings do not have antimicrobial properties or include active pharmaceutical ingredients. Their use in the treatment of purulent wounds and burns mostly limited to high-draining properties, soothing and pain relief, rehydration of the wound bed, and facilitation of autolytic debridement. This work aims to develop a technology for manufacturing novel hydrogel materials with antimicrobial activity for application as a flat sheet-type wound dressings. These products will be useful for treating various skin abrasions or burns, inflammatory skin diseases and chronic wounds. The use of antimicrobial dressings can reduce the need for antibiotics and therefore concerns about antibiotic resistance.

Hydrogels are natural or synthetic hydrophilic materials with cross-linked structure, capable of holding large amounts of water (up to 1-2 liters of water per 1 g of dry polymer) without complete dissolution. The ability of hydrogels to absorb water arises from the presence of hydrophilic functional groups present in these materials, while their resistance to dissolution arises from cross-links between network chains. Hydrogels are soft and porous materials, resembling soft biological tissues. They are able to donate water to dehydrated tissue, while allowing the passage of water vapour and oxygen to the wound surface. This helps to increase the phagocytic activity of leucocytes and enzymatic activity of damaged cells. This, in turn, removes necrotic tissue during the autolysis, a destructive phase of wound healing. Due to this unique combination of physicochemical and biological properties hydrogel materials have found numerous biomedical applications, including wound care, contact lenses, hygiene products, drug delivery systems and tissue engineering [1].These materials provide moisture to the wound, which promotes granulation, epithelialisation, and autolytic debridement; they also facilitate reduction of pain. Hydrogel dressings have many advantages over traditional oil and fat based ointments and creams. In particular, they can provide an active cleansing of wounds due to draining effects; they have excellent compatibility with a variety of drugs; they could be easily and painlessly removed from the wound surface. These properties of hydrogel wound dressings can effectively promote skin repair to treat abrasions, burns, skin inflammation, ulcers, including diabetic skin and feet.

Radiation crosslinking of polymers is one of the established methods of manufacturing hydrogels for wound care applications [2]. This method offers a number of advantages, including the simultaneous cross-linking and sterilisation of the final product. The Institute of Nuclear Physics (Kazakhstan) uses this radiation technology for producing hydrogel wound dressings. The present project will focus on the development of novel formulations for producing hydrogel wound dressings, which will include an additional polymeric ingredient – chitosan. Chitosan is a commercially-available cationic polysaccharide that exhibits excellent antimicrobial [3], bioadhesive [4] and wound healing properties [5].

In the present work the variety of formulations of hydrogel dressings were produced by the Institute of Nuclear Physics from aqueous solutions of gel-forming polymer (GP) polyvinylpyrrolidone (PVP), agar as a thickener, chitosan, $AgNO_3$, and polyethylene glycol (PEG) as a plasticizing agent. The photo of synthesized hydrogel wound dressings is shown in Figure 1. The following parameters were varied for the synthesis of hydrogel dressings containing chitosan with antimicrobial activity and with optimal properties (Table 1-2).

Figure 1. The photo of synthesized hydrogel wound dressings based on polyvinylpyrrolidone, agar, chitosan and polyethylene glycol as a plasticizing agent.

Table 1 - Composition of hydrogel wound dressings based on Chitosan and Agar.

№	Composition Chitosan-Agar (%)	Chitosan (%)	Agar (%)	PVP (%)	PEG (%)
1	1.25-0.05	1.25	0.5	7.0	1.5
2	1.25-0.10	1.25	1.0	7.0	1.5
3	1.25-0.15	1.25	1.5	7.0	1.5
4	1.25-0.20	1.25	2.0	7.0	1.5
5	1.2-0.0	1.2	0.0	7.0	1.5
6	2.2-0.0	2.2	0.0	7.0	1.5
7	0.0-1.0 (Aqua Dress)	0.0	1.0	7.0	1.5

Table 2 - Composition of hydrogel wound dressings based on chitosan, agar and $AgNO_3$

№	Composition Chitosan-Agar (%)	PVP (%)	PEG (%)	$AgNO_3$ (%)	Dose, kGy
1	1.25-0.20, HMW	7.0	1.5	-	21.80
2	1.25-0.20, HMW	7.0	1.5	-	17.80
3	1.25-0.20, HMW	7.0	1.5	-	13.82
4	1.25-0.20, AMW	7.0	1.5	10	13.82

5	1.25-0.20, HMW	7.0	1.5	10	21.80
6	1.25-0.20, HMW	7.0	1.5	10	17.80
7	1.25-0.20, HMW	7.0	1.5	10	13.82
8	0-1.0 (Aqua Dress)	7.0	1.5	10	21.80

*HMW – High molecular weight of chitosan; AMW – Average molecular weight of chitosan.

For synthesized hydrogel wound dressings the swelling characteristics, mechanical test and adhesion tests and antimicrobial activities have been studied. The data obtained from swelling characteristics analysis showed that the presence of ionic component in the formulation results in better ability of hydrogels to absorb water what is attractive because it can provide better perfomance of hydrogel dressings. The samples with highest chitosan content are mechanically weak and variation of chitosan and agar ratio allows selecting optimal formulation content. Thus, new hydrogels can provide better drainage effect due to the higher swelling degree. Nevertheless, higher content of chitosan in the hydrogels leads to a decrease in the pH value to 4.5 (for formulations with completely substituted agar) and pH 5.2 (for formulations with chitosan and agar 1.25-0.20 weight %). These values are close to the allowable pH range for wound dressings. Institute of Nuclear Physics (INP) produces hydrogel dressings with typical pHs around 5.5. Another interesting feature is the possibility to substitute agar completely or partially - with chitosan as a thickener. It will allow a decrease in the hydrogel dressing cost because chitosan is cheaper than agar.

Mechanical properties and adhesiveness of the wound dressings to the skin were studied using Texture Analyzer. The hydrogel wound dressings "Aqua Dress" produced by INP have been used to compare the properties of newly synthesized chitosan dressings. The mechanical properties of the "Aqua Dress" dressings showed higher mechanical properties comparing to hydrogel wound dressings with chitosan. However, synthesized new dressings possess moderate mechanical properties, which have been improved by addition of $AgNO_3$ in the formulation. Adhesiveness test showed that new dressings have better adhesiveness to the skin compared to "Aqua Dress" hydrogels without chitosan.

During the study of antimicrobial properties of dressings the chitosan containing samples did not show any antimicrobial activity probably because of relatively high pH value and as a result - not sufficient ionization degree of chitosan functional groups. Addition of $AgNO_3$ in the formulation provided antimicrobial activity of hydrogels and improving the mechanical properties of wound dressings because Ag ions form silver nanoparticles, structuring the polymer network and play a role of additional crosslinking agent.

Acknowledgments

This work financially supported by the Royal Academy of Engineering via Industry Academia Partnership Programme (IAPP\1516\27).

References

1. Calo E., Khutoryanskiy V.V. Biomedical applications of hydrogels: A review of patents and commercial products, European Polymer Journal. - 2015, 65. – p.252
2. Rosiak J.M. Radiation formation of hydrogels for drug-delivery, Journal of Controlled Release. - 1994, 31. – p.9

3. Gottenbos B., van der Mei H.C., Klatter F., Grijpma D.W., Feijen J., Nieuwenhuis P., Busscher H.J. Positively charged biomaterials exert antimicrobial effects on gram-negative bacilli in rats, Biomaterials. – 2003. - 24 (16). – p.2707
4. Khutoryanskiy V.V. Advances in Mucoadhesion and Mucoadhesive Polymers, Macromolecular Bioscience. - 2011, 11. – p.748
5. Azuma, J. Funct. Biomater. 2015, 6, - p.104