SUMMARY

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Polymeric nanofibers have demonstrated great potential as a platform for many biomedical applications due to their unique properties such as high porosity, strong mechanical properties, , high surface area in addition to their ability for incorporating drugs or bioactive factors for sustained release and localized drug delivery. The combined features of nanofibrous matrices promoted their use for wound healing, anti-tissue adhesion, tissue engineering and other biomedical applications.

Applying the principles of drug delivery technology, we aimed to develop an a novel anti-microbial-loaded nanofibers for the application in various biomedical applications such as promoting healing of infected wounds, prevention or reduction of post-surgical tissue adhesion and development of medicated stents, sutures and other implants. The selected drug was methylene blue that exerts antimicrobial activity that can be enhanced by application of light in what is called Antimicrobial Photodynamic Therapy (APDT) .The current thesis is presented in four chapters.

1. Chapter One: Development of novel methylene blue-loaded polyhydroxybutyrate nanofibers for biomedical applications

This chapter was concerned with the development of methylene blue (MB)-loaded polyhydroxybutyrate (PHB)-based nanofibers that would be used for two different biomedical applications throughout the thesis. The developed fibrous matrices were then examined for their anti-tissue adhesion effect (in Chapter Two). Enhancement of the antimicrobial by the aid of APDT was examined (in Chapter Three) and used (in Chapter Four) as wound dressing for infection control and enhancement of wound healing

Novel MB-loaded PHB-based nanofibers were prepared by emulsion electrospinning with targeted pharmaceutical attributes in terms of drug incorporation efficiency, release pattern and degradability. The effect of experimental variables including: emulsion formulation, polymer concentration and drug loading on morphology, incorporation efficiency and release were investigated. Attempts to modulate the behavior of the developed systems including blending with PEG 4000 were done. The developed nanofibers were characterized by using SEM, DSC, FT-IR, and assessment of drug entrapment efficiency, drug release and polymer degradation. Different formulas have been developed with high incorporation efficiency and average fiber diameter ranging from 400 to 600 nm for the MB loaded ones. Two of them have been selected for further biological applications. They were MB-loaded PHB and PHB/PEG (60/40) nanofibers. They both have high incorporation efficiency almost 100% but they differ in term of hydrophilicity, drug release behavior and matrix degradation. They were designed for two different biomedical applications. As the hydrophilic formula showed a faster initial drug release that could prevent the proliferation of early intruding bacteria, it was tested for its antibacterial activity *in vitro* against 2 bacterial strains; MRSA and *S.aureus.* The effect of the antibacterial nanofibers on bacteria was investigated by viable count technique. The effect of electrospinning on drug antibacterial activity was assessed using the agar diffusion method and proved that MB activity was not affected during the drastic environment of electrospinning.

2. Chapter Two: Tissue anti-adhesion potential of selected polyhydroxybutyrate biomaterials in a rat model

Chapter two was concerned with the investigation of the ability of PHB-based membranes to reduce the post-surgical peritoneal adhesion induced in rat model. MB can induce dual effect for prevention of tissue adhesion through its antimicrobial effect and the direct anti-tissue adhesion effect. So, MB-loaded nanofibers exert a dual effect for reduction of adhesion; as a physical barrier and as a carrier of anti-adhesive pharmacological adjuvant. The formed adhesions were assessed macroscopically through scoring in terms of type, tenacity and extent of adhesion bands formed , and by histological examination .While, the implants retrieved after animal scarification were assessed for changes in their physical properties and microscopically by SEM to examine cell growth and attachment to their surfaces. The results showed a good ability for PHB nanofibers to reduce the formation of adhesion bands, while PHB/PEG blended nanofibers were not recommended for the anti-tissue adhesion application, as the leaching of PEG allows for larger pore formation and cell infiltration; however this property is excellent for tissue engineering scaffold applications. However, it was observed that loading of PHB/PEG nanofibers with MB rendered it able to reduce tissue-adhesion formation. The striking reduction in peritoneal adhesion was obtained by using MB-loaded film. The smooth surface of the film completely prevent cell adherence as examined by SEM. The histological examination of the injured tissue showed a great reduction in inflammation and leukocytes infiltration. That result was further assured by differential WBCs count in peripheral blood that showed neutropenia.

3. Chapter Three : Methylene blue-eluting nanofibers as a potential biomaterial for antimicrobial photodynamic therapy (APDT)

Chapter three aimed to enhance the antibacterial activity of MB-loaded nanofibers by the application of activating red light for APDT. The developed system consisted of the MB-loaded nanofibers and the light of optimum wavelength and fluence were examined for its *in vitro* photobioactivity. Its response to light was assessed by measuring light transmission through the fibrous matrix which showed opaque nature that could protect the encapsulated photosensitizer. For MB to be activated by light, it should be first released from the matrix. The effect of light fluence on singlet oxygen production by the released MB was assessed using uric acid as a quenching agent. Increasing the light fluence up to 300 J/cm^2 would result in more singlet oxygen production which has antibacterial destroying effect. MB-loaded nanofibers were tested for their photodynamic antibacterial activity using red LED at 650 nm which revealed bactericidal activity. Antimicrobial profile of the light activated nanofibers revealed that the tailored MB release profile is well suited with a high initial burst proved to be sufficient for the application of APDT then a slower release rate that did maintain the antibacterial effect of MB in dark.

4. Chapter Four : Methylene blue-eluting nanofibers for antimicrobial photodynamic therapy (APDT) of infected wounds in immunocompromized rats

APDT has an advantage over the traditional treatment by antibiotics, in term of no development of antimicrobial resistance. PHB/PEG nanofibers provide the required properties to enhance wound healing in terms of high hydrophilicity, fluid uptake and good cell

attachment. So, MB-loaded nanofibers would provide a unique dual effect which made it necessary to test it against a challenging model of infected wound. *S. aureus* infected wounds were induced in cyclosporine A- immunosuppressed rat model. Wounds were irradiated with red LED at 650 nm after eluting a suitable amount of MB from the fibrous mats. The wound healing properties of MB-loaded PHB/PEG nanofibers was assessed by microbiological and morphological examination. Application of MB-loaded nanofibers with multiple irradiation resulted in accelerated wound healing of better quality and no scar formation on the macroscopic scale. The results are due to enhanced re-epithelization and granular tissue formation as revealed by histological examination. APDT has also succeeded to eradicate the infective bacteria. At the molecular level, examination of VEGF, PDGF, COX-2 and TNF-α levels by RT-PCR showed a great potential of MB-loaded PHB/PEG NFs combined with APDT to enhance wound healing.

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الملخص العربى

لقد مهدت أنظمة توصيل الدواء البلمرية الطريق لمعظم التطبيقات الطبية الحيوية الواعدة والتكنولوجيا الحيوية. ومن بين تلك التطبيقات، الأنظمة الموضعية التي تلعب دورا هاما فيما يتعلق بالتوصيل الموضعي للدواء في العديد من الأمراض الجلدية، والعلاج الكيميائي بعد الجراحات الموضعية، وعلاج الجروح والحالات المرتبطة بها والوقاية من التصاقات الأنسجة بعد الجراحة، ودعم وتوجيه نمو الخلايا في تطبيقات هندسة الأنسجة. وفي هذا الإطار، أثبتت الأبحاث على الألياف البلمرية النانونية بخصائصها الفريدة خلال العقد الماضي إمكانية إستخدامها كأساس لكثير من التطبيقات الطبية الحيوية. ومن أهم هذه الخصائص ارتفاع نسبة المسامية واتساع مساحة السطح والقوة الميكانيكية إضافة إلى إمكانية توظيفها كنظام موصل موضعي للأدوية والمواد النشطة بيولوجيا والتحكم الزمني في انطلاقها.

الهدف من الرسالة

تهدف الرسالة إلى تطوير نوع جديد من الألياف البلمرية النانونية المغزولة كهربيا والمضادة للجراثيم دون زيادة المقاومة الجرثومية والقابلة للتنشيط الضوئي في التطبيقات الطبية الحيوية الموضعية وذلك للمساهمة في تحسين المردود العلاجي في هذه التطبيقات. اعتمد تحقيق هدف الرسالة على الجمع بين الخصائص التركيبية والوظيفية للألياف النانونية كنظام حامل لتوصيل الدواء ودعامة ميكانيكية لنمو الخلايا وغشاء حاجز لمنع التصاق الأنسجة بعد العمليات الجراحية وكذلك التأثيرات الحيوية المجتمعة للميثيلين الأزرق كمضاد للجراثيم دون زيادة مقاومتها ومحفز ضوئي قادرعلى تعزيز المفعول المضاد للجراثيم عند التعرض للضوء (وهو أساس ما يعرف بالعلاج الضوئي المضاد للجراثيم) إضافة إلى تأثيرات حيوية أخرى.

تقع الرسالة في أربعة فصول تتناول تطوير ألياف بلمرية نانونية وتوصيفها وتقييم إستخدامها في الحد من التصاقات الأنسجة بعد العمليات الجراحية في نموذج الفئران وكمواد حيوية مضادة للجراثيم بالتعزيز الضوئي لعلاج الجروح الاستئصالية الملوثة في نموذج الفئران المثبطة المناعة.

الفصل الأول:

تطوير ألياف نانونية من عديد هيدروكسى البيوتيرات محملة بالميثيلين الأزرق للتطبيقات الطبية الحيوية

تناول هذا الفصل تطوير ألياف نانونية مصنعة بطريقة الغزل الكهربي من بلمر عديد هيدروكسى البيوتيرات وتحميلها بالميثيلين الأزرق وذلك بغرض توظيف النسيج الليفي الناتج في تطبيقات طبية حيوية مختلفة. تم إستخدام طريقة الغزل الكهربى للمستحلب لتحضيرالألياف نظرا لذوبانية الميثيلين الأزرق في الماء كما تم مزج عديد هيدروكسى البيوتيرات الكاره للماء مع عديد الإثيلين جليكول ٤٠٠٠ المحب للماء للحصول على ألياف نانونية مقبولة من حيث الشكل والحجم وذات خصائص متباينة من حيث كفاءة تحميل ومعدل انطلاق المادة الفعالة والقدرة على امتصاص الماء. ولذلك فقد تم دراسة تأثير تركيب المستحلب وتركيز البلمر ونسبة التحميل الأولي للمادة الفعالة على خصائص الألياف المبينة عاليه. تم توصيف الألياف بإستخدام المجهر الإلكتروني الماسح وطرق التحليل الحراري التفاضلي والأشعة تحت الحمراء وتعيين نسبة كفاءة التحميل بالمادة الفعالة ومعدل انطلاقها من الألياف وكذلك سرعة تحلل الألياف معمليا. بينت النتائج أن متوسط قطر الألياف تراوح بين ٤٠٠ و ٦٠٠ نانومترا

وأنها تميزت في مجملها بكفاءة تحميل مرتفعة وصلت إلى ١٠٠٪ في بعض التركيبات. وبناء على هذه النتائج، تم اختيار نوعين من الألياف لمزيد من التوصيف هما الألياف النانوية المصنعة من عديد هيدروكسى البيوتيرات ومزيج عديد هيدروكسى البيوتيرات وعديد الإثيلين جليكول بنسبة ٤٠/٦٠. يتميز النوع الأول بانطلاق أولي سريع نسبيا للميثيلين الأزرق وبطء التحلل في الماء وهو مناسب للتطبيقات الطبية الحيوية طويلة المدى نسبيا والتى تستلزم عدم التحلل السريع للنسيج الليفي مثل الخيوط الطبية والأغشية المانعة لالتصاق الأنسجة بعد عمليات البطن. أما النوع الثاني فهو مناسب للتطبيقات المضادة للجراثيم الأقصر مدى مثل علاج الجروح والتي تستلزم تحكما زمنيا ثنائي الطور في انطلاق المادة الفعالة بحيث يمكن السيطرة على العدوى الجرثومية مبكرا في الجرح مع استمرار هذه السيطرة طوال الفترة اللازمة لالتئام الجرح. وباختبار النشاط المضاد للجراثيم لهذين النوعين من الألياف معمليا بإستخدام سلالتين بكتيريتين هما البكتريا العنقودية الذهبية المقاومة للمسيثيللين (MRSA) والبكتريا العنقودية الذهبية (Staphylococcus aureus)، تبين عدم تأثر النشاط المضاد للبكتيريا للميثيلين الأزرق بالتعرض لظروف الغزل الكهربي للألياف (بإستخدام طريقة الانتشار في الأجار) و قدرة الألياف المحملة بالميثيلين الأزرق على مقاومة البكتيريا (بإستخدام تقنية العد).

خلص هذا الفصل إلى إمكانية إستخدام ألياف عديد هيدروكسى البيوتيرات ومزيج عديد هيدروكسى البيوتيرات وعديد الإثيلين جليكول النانونية المحملة بالميثيلين الأزرق في تطبيقات طبية حيوية مختلفة مضادة للجراثيم .

.الفصل الثاني:

قدرة مواد حيوية مختارة من عديد هيدروكسى البيوتيرات للحد من التصاق الأنسجة فى الفئران

تناول هذا الفصل دراسة قدرة الألياف النانوية المصنعة من بلمر عديد هيدروكسي البيويترات منفرداً أو من مزيج بلمري مكون من ذات البلمر مع عديد الإيثيلين جليكول ٤٠٠٠ والمحملة بمادة الميثيلين الأزرق كمادة مضادة للأكسدة والجراثيم، علي الحد من التصاق الأنسجة البريتونية بعد العمليات الجراحية وذلك بإستخدام نموذج التصاق المعي الأعور وجدار البطن في إناث الفئران. تم تقييم الالتصاقات المتكونة بعد الجراحة بإستخدام مقياس متعارف عليه لتوصيفها من حيث درجة الانتشار والقوة المطلوبة لفصل الالتصاقات والخصائص التشريحية للأنسجة المتكونة. فضلا عن ذلك، تم تقييم طبيعة التئام الأنسجة مابعد الجراحة ودرجة تليف أنسجة الالتصاقات من خلال التحليل النسيجي لهذه الأنسجة. تشتمل الدراسة على جزئين. تم في الجزء الأول تقييم قدرة الألياف النانونية المحضرة من كل من عديد هيدروكسي البيوتيرات منفردا ومن المزيج البلمري، المحملة بالميثيلين الأزرق بكمية تسمح بجرعة مقدارها ٢,٥ مجم/كجم، كأغشية مانعة للالتصاقات ما بعد الجراحة وذلك بإستخدام عدد من المعالجات الضابطة. أظهرت النتائج قدرة أكبر للألياف النانويه المصنعة من عديد هيدروكسي البيوتيرات علي الحد من الالتصاقات البريتونية مقارنة بتلك المحضرة من المزيج البلمري. أعزي الفرق إلى ارتشاح عديد الإيثيلين جليكول القابل للذوبان في الماء مما يؤدي إلى زيادة مسامية الألياف وتسلل ونمو الخلايا داخلها وهو ما أكده فحص الألياف النانونية المستخرجة من التجويف البريتوني في نهاية الدراسة بواسطة المجهرالإلكتروني الماسح والذى أظهر زيادة في مسامية الألياف المحضرة من المزيج البلمري ونموا واضحا للخلايا فيها مقارنة بنمو محدود للخلايا علي سطح ألياف عديد هيدروكسي البيوتيرات. أثبتت الدراسة أن تحميل الألياف محل الدراسة بالميثيلين الأزرق، ولاسيما الألياف المحضرة من المزيج البلمري والتي تسمح بانطلاق بالميثيلين الأزرق بمعدل أسرع يعزز نسبيا من قدرتها علي الحد من الاتصاقات مما يشير إلى أهمية توافر المادة الفعالة بتركيز موضعي كاف في المرحلة المبكرة بعد الجراحة.بينت نتائج الجزء الأول من الدراسة أن هناك حاجة لتحسين أداء المواد الحيوية المعتمدة على عديد هيدروكسي البيويترات كحاجز مانع لالتصاقات الأنسجة البريتونية وأن هذا

التحسين يتطلب إستخدام حاجز ذي تركيب بلمري منخفض المسامية ولا يسمح بزيادة كبيرة في المسامية في الوسط البيولوجي (مما أدى إلى استبعاد المزيج البلمري) إضافة إلى زيادة في جرعة المثيلين الأزرق. وقد أخذت استنتاجات الجزء الأول من الدراسة في الاعتبار عند تصميم الجزء الثاني الذي تم الاعتماد فيه على أغشية من عديد هيدروكسى البيوتيرات مانعة للالتصاقات مكونة إما من ألياف نانونية مغزولة كهربيا أو أغشية غير ليفية ذات تركيب مماثل محضرة بطريقة الصب كما تم زيادة التحميل بالمثيلين الأزرق لإتاحة جرعة مقدارها ٢٠ مجم/كجم، جزء منها محمل سطحيا لضمان انطلاق سريع للمادة الفعالة، وذلك بإستخدام التجارب الضابطة اللازمة. أظهرت نتائج الفحص بالمجهر الإلكترونى الماسح والفحص التشريحي للالتصاقات وتعيين عدد كرات الدم البيضاء في عينات من دم الفئران تفوقا ملحوظا للغشاء غير الليفي المحضر بالصب والمحمل بالمثيلين الأزرق في الحد من الالتصاقات البريتونية والالتهابات ما بعد الجراحة.وقد أرجع عدم نمو الخلايا على هذا الغشاء إلى ملاسة السطح وقلة المسامية وسرعة انطلاق المثيلين الأزرق. تشير النتائج إلى ضرورة إجراء المزيد من الدراسات لتقييم قدرة المواد الحيوية المعتمدة على الألياف النانونية مقارنة بالأغشية المصبوبة وذلك تحت نفس الظروف المعملية حيث أن النمط الشائع للدراسات المنشورة يعتمد على تقييم كل نوع على حدة.

الفصل الثالث:

ألياف نانوية مطلقة للمثيلين الأزرق كمادة حيوية محتملة لتطبيقات العلاج الضوئي المضاد للجراثيم

تناول هذا الفصل دراسة إمكانية تعزيز المفعول المضاد للجراثيم للألياف النانونية المحضرة بطريقة الغزل الكهربي للبلمر المكون من مزيج من عديد هيدروكسي البيوتيرات وعديد الإيثيلين جليكول ٤٠٠٠ والمحملة بالميثيلين الأزرق كمحفز ضوئي وذلك عن طريق التحفيز الكيميائي الضوئي بإستخدام الضوء الأحمر (٦٥٠ نانومتر بإستخدام الباعث الضوئي الثنائي). أظهرت نتائج دراسات تقييم نفاذ الضوء من خلال مصفوفة الألياف البلمرية النانونية عدم شفافية هذه الألياف للضوء وضرورة أن يعتمد التحفيز الضوئي على الانطلاق المسبق للميثيلين الأزرق. وبناء على ذلك فقد تم تصميم الدراسة على إستخدام ألياف نانونية تسمح بانطلاق المثيلين الأزرق بنمط ثنائي الطور يتسم بمعدلات إنطلاق أولية عالية، يمكن عن طريق التحفيز الضوئي المتزامن أن تؤدي إلى التثبيط الفوري المبكر لنمو الجراثيم على أن يسمح التحكم الزمني في الطور الثاني في انطلاق أبطء يؤدي إلى استمرار تأثير الميثيلين الأزرق المضاد للبكتيريا في عدم وجود الضوء وذلك اعتمادا على حماية الألياف البلمرية للمثيلين الأزرق المحوصل وعدم تأثر ثباتيته الكيميائية بالتحفيز الضوئي. ولتحديد المدى الأمثل لقوة الضوء المطلوبة لتحفيز المثيلين الأزرق في محلول مائي، تم إستخدام طريقة حمض البوليك كعامل كابح للأكجسين النشط الناتج عن التحفيز الضوئي. وقد وجد أن زيادة قوة الضوء فيما بين ٥٠ إلى ٣٠٠ جول/سم^{٢}يؤدي إلى إنتاج المزيد من الأكسجين النشط مع عدم تأثر إنتاجه بزيادة قوة الضوء إلى٤٠٠جول/سم^{٢}. وبناء عليه تم إستخدام قوة ضوء مقدارها ٥٠-٢٠٠ جول/سم^{٢} في التجارب التالية.

وبدراسة النشاط المضاد للجراثيم لمحلول المثيلين الأزرق بإستخدام سلالات البكتريا العنقودية الذهبية المقاومة للمسيثيللين (MRSA) والبكتريا العنقودية الذهبية (Staphylococcus aureus)، تبين أن التحفيز الضوئي (١٠٠ جول/سم^{٢}) يزيد من نشاط المثيلين الأزرق المضاد للجراثيم وتعتمد هذه الزيادة على تركيز المثيلين الأزرق ومدة الحضانة مع البكتيريا وقد أمكن القضاء على البكتيريا العنقودية الذهبية المقاومة للمسيثيللين (MRSA) تماما بإستخدام محلول المثيلين الأزرق بتركيز ٥٠ مجم/مل ومدة حضانة لا تقل عن ١٥ دقيقة تسمح بانطلاق كمية كافية من المثيلين الأزرق. وباختبار نشاط الألياف النانونية المحملة بالمثيلين الأزرق االمضاد للجراثيم ، تبين أن التحفيز الضوئي (١٠٠ جول/سم^{٢})

للمثيلين الأزرق بعد فترة حضانة ١٥ دقيقة لعينات الألياف في وجود البكتيريا قد أدى إلى القضاء تماما على بكتيريا الMRSA و الحد إلى درجة كبيرة من نمو البكتريا العنقودية الذهبية (Staphylococcus aureus). كما بينت النتائج استمرار النشاط المضاد للجراثيم لفترة دراسة مدتها ٢٤ ساعة بعد التحفيز الضوئي مما يؤكد عدم استعادة البكتيريا لنشاطها وتأثير المثيلين الأزرق الممتد الإنطلاق.

خلص هذا الفصل إلى إثبات إمكانية التحفيز الضوئي للنشاط المضاد للبكتيريا للألياف النانونية المحضرة بطريقة الغزل الكهربي للبلمر المكون من مزيج من عديد هيدروكسي البيوتيرات وعديد الإيثيلين جليكول ٤٠٠٠ والمحملة بالميثيلين الأزرق كمحفز ضوئي ومضاد بكتيري. وبهذا تمثل هذه الألياف قاعدة لنوع جديد من الألياف النانونية تعتمد آلية تحفيزها ضوئيا على انطلاق المحفز الضوئي. تتميز هذه الألياف المعتمة بحماية المحفز الضوئي المحوصل بداخلها من التعرض للضوء في غير أوقات التحفيز المطلوب كما أنها تسمح بمفعول سريع مضاد للبكتيريا بمجرد التحفيز الضوئي ومفعول إضافي ممتد مرتبط بالانطلاق المنضبط للمثيلين الأزرق كمضاد بكتيري. ومن المتوقع أن تجعل هذه الخصائص من الألياف النانونية موضوع الدراسة والتي تجمع بين الخصائص البنائية والوظيفية المتعددة للألياف النانونية وخصائص المثيلين الأزرق كمادة فعالة متعددة التأثيرات الحيوية،مادة حيوية مفيدة في علاج الجروح الملوثة وهو موضوع الفصل الرابع.

الفصل الرابع:

ألياف نانوية مطلقة للمثيلين الأزرق للعلاج الضوئي المضاد للجراثيم للجروح الملوثة فى الفئران المثبطة المناعة

بينت نتائج الفصول السابقة أن الألياف النانوية المصنعة من مزيج عديد هيدروكسى البيوتيرات وعديد الإيثيلين جليكول ٤٠٠٠ و المحملة بالميثيلين الأزرق تتسم بالخصائص المطلوبة لتعزيز إلتئام الجروح وذلك بفضل خواصها المحبة للماء وقدرتها الجيدة على امتصاص السوائل وتسهيل نموالخلايا عليها، إضافة إلى إمكانية تعزيز المفعول المضاد للبكتيريا من حيث الشدة والسرعة بالتحفيز الضوئي. تم اختبار هذه الألياف في علاج الجروح الاستئصالية المصابة بالبكتريا في نموذج الفئران المُثبطة المناعة،والتى تشكل نموذجا متحديا من الجروح. تم إحداث الجروح المصابة بالبكتريا االمكورة العنقودية الذهبية فى نموذج الفئران ذوات المناعة المثبطة بواسطة السيكلوسبورين-أ. وقد تمت إضاءة الجروح بواسطة الضوء الأحمر ذو الطول الموجى ٦٥٠ نانومتر بعد إطلاق كمية مناسبة من المثيلين الأزرق من المصفوفات الليفية. تم تقييم خصائص التئام الجروح بواسطة الألياف عن طريق الفحص الشكلى للجروح وقياس أبعادها والفحص الميكروبيولوجي لمسحات من الجروح والفحص النسيجي لعملية الإلتئام وذلك بإستخدام المعالجات الضابطة اللازمة لتفسير النتائج. أظهرت النتائج قدرة الألياف موضوع الدراسة على تعزيز التئام الجروح ولاسيما بتكرار تعريض الجروح للضوء. أدى العلاج الضوئي المضاد للجراثيم على هذا النحو بإسراع عملية الإتئام والقضاء على البكتيريا المعدية وتحسين جودة الإلتئام نظرا لعدم تكوين ندبة وعودة نمو الشعر. كما تم إستخدام تقنية تفاعل البوليمراز المتسلسل للكشف جينات كل من VEGF, PDGF, COX-2, TNF-α. أظهرت نتائج الدراسة مجتمعة أن إستخدام الألياف النانوية موضوع الدراسة كمادة حيوية لعلاج الجروح مصحوبا بالتحفيز الضوئى المضاد للجراثيم يعد تقنية مزدوجة جديدة فعالة في علاج الجروح صعبة الإلتئام. تتميز هذه التقنية على العلاج التقليدي بواسطة المضادات الحيوية بعدم تطويرسلالات جرثومية مقاومة للعلاج وإمكانية تطويرها لزيادة فعاليتها.

الخلاصة

تم في هذه الرسالة تقديم مواد حيوية معتمدة أساسا على بلمر عديد هيدروكى البيوتيرات وهي ألياف نانونية كارهة للماء مصنعة من عديد هيدروكى البيوتيرات وأخرى أكثرا حبا للماء مصنعة من المزيج البلمري المكون من هذا البلمر وعديد الإثيلين جليكول ٤٠٠٠ وهي ألياف متعددة الوظائف مغزولة كهربيا وذلك بالإضتفة إلى أغشية من عديد هيدروكى البيوتيرات جميعها محملة بمادة المثيلين الأزرق كصبغ مضاد للجراثيم ومضاد للأكسدة ومحفز ضوئي وذلك للإستخدام في تطبيقات حيوية مختلفة. يعتمد إستخدام هذه المواد على خواصها الصيدلانية ولا سيما نمط انطلاق المادة الفعالة منها وتفاعلها مع الخلايا. أمكن إستخدام ألياف عديد هيدروكسى البيوتيرات بطيئة التحلل بعد تعديل مواصفاتها في الحد من الالتصاقات البريتونية بعد الجراحة في الفئران إلا أن كفائتها كانت أقل من أغشية غير ليفية بنفس التكوين محضرة بطريق الصب. كما أمكن إستخدام ألياف نانونية محضرة من المزيج البلمري محملة بالمثيلين الأزرق مع طريقة التحفيز الضوئي كتقنية مزدوجة جديدة لعلاج الجروح تعتمد على انطلاق المحفز وإثبات فعالية هذه التقنية في علاج الجروح صعبة الالتئام في الفئران. تعتبر المواد الحيوية المقدمة في هذه الرسالة إضافة هامة للتطبيقات الطبية الحيوية المضادة للجراثيم لا تؤدي إلى تكوين سلالات مقاومة من الجراثيم يمكن أن تكون بديلا لإستخدام الأنظمة المعتمدة على المضادات الحيوية مما يساعد في ترشيد إستخدام المضادات الحيوية.

إقرار

أقر أنه لا يوجد أى جزء من هذا العمل قد سبق تقديمه لنيل درجة أخرى فى هذه الجامعة أو أى معهد أو مؤسسة تعليمية أخرى

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جامعة الإسكندرية

كلية الصيدلة

قسم الصيدلانيات

" دراسة صيدلانية لأنظمة توصيل بلمرية لتطبيقات طبية حيوية موضعية "

رسالة مقدمة من

نسمة السيد أحمد أحمد إبراهيم

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جامعة الإسكندرية

كلية الصيدلة

قسم الصيدلانيات

" دراسة صيدلانية لأنظمة توصيل بلمرية لتطبيقات طبية حيوية موضعية "

رسالة مقدمة

لقسم الصيدلانيات – كلية الصيدلة – جامعة الاسكندرية

كجزء من متطلبات درجة

الماجستير

فى

العلوم الصيدلية (الصيدلانيات)

من

نسمة السيد أحمد أحمد إبراهيم

بكالوريوس فى العلوم الصيدلية ٢٠٠٧
كلية الصيدلة
جامعة الاسكندرية

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