8th Iranian & 3rd Middle East Controlled Release Society Virtual Congress

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Professor Morteza Rafiee Tehrani
Pharm.D., ph.D.

Chief Executive:

Dr. Ehsan Aboutaleb
Pharm.D., ph.D.

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Iranian Controlled Release Society

Chairman's Message:

In the name of God
On behalf of Controlled Release Society of Iran, it was our pleasure to have you all part of the 3rd Middle East Conference and 8th Iranian Controlled Release Congress. We were honored to host this congress for controlled release scientists and researchers. Many participants from international and Iranian universities and scientific institutes were participated in this congress. We had a great participation and we hope you would have enjoyed your attendance at Iranian Controlled Release Congress and hope to see you all in our next Congress to be held in 2024.

Yours sincerely,
Professor M. Rafiee-Tehrani
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Chairman of the 8th ICRC and 3rd MECRC conference

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ICRC 2022/MECRC 2022 Program
May 9-11, 2022

First Day, Monday 2022/May/9			
Main Speakers	**Lecture Title**	**Lecture Start Time**	**Duration(Min)**
Morteza Rafiee Tehrani	**Welcoming Message**	**9:30 GMT (13:00 Tehran)**	**10 minutes**
Farid Abedin dorkoosh	**A novel pulsatile drug delivery of teriparatide**	**9:40 GMT (13:10 Tehran)**	**40 minutes**
Andreas Bernkop-Schnürch	**Thiolated cyclodextrins**	**10:20 GMT (13:50 Tehran)**	**40 minutes**
Mohamed Elsawy	**Smart biomaterials in Drug delivery and regenerative medicine Peptides: A platform for innovation of biomaterials**	**11:00 GMT (14:30 Tehran)**	**30 minutes**
Payam Khazaeli	**Sialic acid decorated chitosan-selenium nanostructures: Statistical optimization of production, characterization, and assessment of cytotoxic effect against two glioblastoma cell lines**	**11:30 GMT (15:00 Tehran)**	**30 minutes**
Navid Neyshaburinezhad	**A review of diamond nanoparticles and their applications in pharmacy and medicine**	**12:00 GMT (15:30 Tehran)**	**30 minutes**
Break			**10 minutes**
Oral Presenters	**Title**	**Start Time**	**Duration(Min)**
Mohaddeseh sadat moosavi	Preparation and Characterization of	12:40 GMT	15 minutes

	Quercetin-Loaded Polyvinyl Alcohol-Tannic Acid as a Biocompatible and Biodegradable Implant	(16:10 Tehran)	
Hamidreza Arabloo	Formulation and evaluation of meprazole-Chitosan microparticles coated with Eudragit prepared by spray drying for making suspension	12:55 GMT (16:25 Tehran)	15 minutes
Mahsa Akbari	Fabrication of a dissolvable photothermal polymeric microneedle containing bismuth nanoparticles for cancer therapy	13:10 GMT (16:40 Tehran)	15 minutes
Homa Faghihi	Formulation and Processing of Dry Powders of Trastuzumab via Spray Freeze Drying and Evaluation of Physicochemical Properties and Stability	13:25 GMT (16:55 Tehran)	15 minutes
Break			**10 minutes**
Fatimah Hasan shakir	Preparation and characterization of chitosan hydrogel loaded by ZnO nanoparticle and Vancomycin: Potential carrier in antimicrobial therapy	13:50 GMT (17:20 Tehran)	15 minutes
Hasanain AL-awadi	Preparation and evaluation of chitosan/aloe vera gel loaded by ZnO nanoparticles for wound healing	14:05 GMT (17:35 Tehran)	15 minutes
Amin Haghighat Naeini	Minoxidil-loaded methylated aminobenzyl carboxymethyl chitosan nanoparticles: Physicochemical characterization	14:20 GMT (17:50 Tehran)	15 minutes
Samin Abbaszadeh	A Multifunctional Photoactive Hydrogel Containing Bismuth Sulfide Nanoparticles for Synergic Photo-Chemo-Immunotherapy of Cancer	14:35 GMT (18:05 Tehran)	15 minutes

ICRC 2022/MECRC 2022 Program
May 9-11, 2022

Second Day, Tuesday 2022/May/10			
Main Speakers	**Lecture Title**	**Lecture Start Time**	**Duration(Min)**
Rassoul Dinarvand	**The application of controlled delivery systems in neural stem cell proliferation and differentiation**	**9:30 GMT (13:00 Tehran)**	**40 minutes**
Fatemeh Atyabi	**Exosomes, vesicles for drug delivery and cancer therapy**	**10:10 GMT (13:40 Tehran)**	**20 minutes**
Mohammed Taher	**Proniosome delivery of aceclofenac using different carriers**	**10:30 GMT (14:00 Tehran)**	**40 minutes**
Abbas Pardakhty	**Nanovesicle/nanominerals for theranostic applications: A brief review**	**11:10 GMT (14:40 Tehran)**	**30 minutes**
Hamid Reza Moghimi	**Chemical modification, a feasible approach for transdermal peptide delivery**	**11:40 GMT (15:10 Tehran)**	**30 minutes**
Break			**10 minutes**
Oral Presenters	**Title**	**Start Time**	**Duration(Min)**
Parisa Zanjanian	Preparation and evaluation of berberinephospholipid complex to improve its dissolution properties	12:20 GMT (15:50 Tehran)	**15 minutes**
Sahar Mohammad Alizadeh	lipid nanoparticles as a potential tool to overcome antimicrobial resistance	12:35 GMT (16:05 Tehran)	**15 minutes**
Kiyan Musaie	A Hemostatic Injectable Photothermally-Active Hydrogel Prepared via Metal-Coordinated Crosslink for Wound Healing and Cancer Therapy	12:50 GMT (16:20 Tehran)	**15 minutes**
Break			**10 minutes**
Huriya Mohammadnejad	Photothermally Active pH تResponsive Polydopamine@ MnO2 Nano - platform Encapsulated into Platelet Cell Membrane for Multifunctional Cancer Ablation	13:15 GMT (16:45 Tehran)	**15 minutes**
Mahtab Bahmani	Prediction of the IC50 of pyridine crystal Materials on the Basis of their Molecular Structures: Novel architecting for anti-cancer drugs	13:30 GMT (17:00 Tehran)	**15 minutes**
Mohaddeseh	Development of a novel solid lipid	13:45 GMT	**15 minutes**

Shayganpour	nanoparticle based system for enhanced in vivo topical anti-inflammatory activity	(17:15 Tehran)	
Naghmeh Jabarimani	Synthesis and Characteristic of Trimethyl Chitosan nanoparticles coated with polyelectrolyte for RNAi delivery	14:00 GMT (17:30 Tehran)	**15 minutes**
Break			**10 minutes**
Zahra Gharehdaghi	Evaluation of anti-bacterial effect of Polymeric Nanofiber Enriched With piperineon staphylococcus epidermidis biofilm	14:25 GMT (17:55 Tehran)	**15 minutes**
Ayda Mahdavi	Anticancer effect of colchicine-entrapped noisome on MCF-7 breast cancer cells	14:40 GMT (18:10 Tehran)	**15 minutes**
Mohammad Amin Raeisi Estabragh	Alpha-Lipoic Acid niosomes: Formulation physicochemical evaluation and protection effects on cerebral ischemic reperfusion injury in rat model	14:55 GMT (18:25 Tehran)	**15 minutes**
Mahsa Abizadeh	Colchicine entrapped nanoparticle: A strategy to enhance the anticancer effect of cholchicine on MCF-7 breast cancer cell line	15:10 GMT (18:40 Tehran)	**15 minutes**

ICRC 2022/MECRC 2022 Program
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Third Day, Wednesday 2022/May/11			
Main Speakers	**Lecture Title**	**Lecture Start Time**	**Duration(Min)**
Hamid Akbari Javar	**Application of artificial intelligence in pharmacy, from drug discovery to formulation**	**9:30 GMT (13:00 Tehran)**	**40 minutes**
Ehsan Aboutaleb	**Application of artificial intelligence in predicting the pharmacokinetics of drugs**	**10:10 GMT (13:40 Tehran)**	**30 minutes**
Farhan Jalees Ahmad	**Lymphocyte membrane camouflaged Nanoparticles for Novel combination therapy**	**10:40 GMT (14:10 Tehran)**	**30 minutes**
Sara Bahrainian	**Design of graphene-based smart platforms for combined therapy**	**11:10 GMT (14:40 Tehran)**	**20 minutes**
Bijan Malaekeh	**PEGylated solid lipid nanoparticles functionalized by aptamer for targeted delivery of docetaxel in mice bearing C26 tumor**	**11:30 GMT (15:00 Tehran)**	**15 minutes**
Break			**10 minutes**
Oral Presenters	**Title**	**Start Time**	**Duration(Min)**
Mina Mohamadi	Fabrication of hybrid Scaffolds based on hyaluronic acid/gelatin/chitosan/diatom for bone tissue regeneration	11:55 GMT (15:25 Tehran)	15 minutes
Saman Rezaei	Bioinspired Highly Strong, Porous and Photoactive Cellulosic Scaffold for Bone Regeneration	12:10 GMT (15:40 Tehran)	15 minutes
Morteza Abazari	Development of antibacterial and highly protective facemask for prevention of COVID-19 infection	12:25 GMT (15:55 Tehran)	15 minutes
Jafar Asgharpour khoei	Preparation and evaluation of chitosan gel containing Ficus carica extract	12:40 GMT (16:10 Tehran)	15 minutes
Break			**10 minutes**
Khashayar Sanemar	Development, statistical optimization and in vitro/in vivo characterization of an intelligent hydrogel Containing methylated N-(4-N , N-dimethylaminobenzyl) chitosan for glucose responsive insulin delivery	13:05 GMT (16:35 Tehran)	15 minutes
Nika Rezvanjou	Preparation and In vitro / In vivo evaluation of an intelligent drug	13:20 GMT (16:50 Tehran)	15 minutes

	delivery system composed of a hydrogel prepared from 4-N,N-dimethyl aminobenzyl chitosan for glucose-responsive delivery of repaglinide		
Sepideh hassannezhad	Effects of formulation composition on the characteristics of orodispersible films prepared by semisolid extrusion 3D printing	13:35 GMT (17:05 Tehran)	15 minutes
Tara Samizadegan	Formulation and Evaluation of stealth liposomal fluoxetine on memory and cognition performance	13:50 GMT (17:20 Tehran)	15 minutes
Break			**10 minutes**
Saeedeh Ahmadipour	Nanocrystalization of Pioglitazone by Precipitation Method	14:15 GMT (17:45 Tehran)	15 minutes
Kosar Mahdavipour	Development of Finasteride loaded and Minoxidil loaded Chitosan nanoparticles as a Potential carriers for local drug delivery in alopecia	14:30 GMT (18:00 Tehran)	15 minutes
Reihaneh Farajollah	Synthesis, Characterization, and in vitro evaluation of a bio star-hyperbranched polyurethane film based on D-glucose-poly (3-hydroxybutyrate-co-3-hydroxyvalerate) for sustained release of insulin	14:45 GMT (18:15 Tehran)	15 minutes
Vahideh Nosrati	Injectable Photothermally Active Hydrogel Incorporated with CuO Nanosheets for Simultaneous Skin-Tumor Therapy, and Multidrug-Resistant Infection- Induced Wound Healing	15:00 GMT (18:30 Tehran)	15 minutes

Preparation and Characterization of Quercetin-Loaded Polyvinyl Alcohol-Tannic Acid as a Biocompatible and Biodegradable Implant

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Introduction

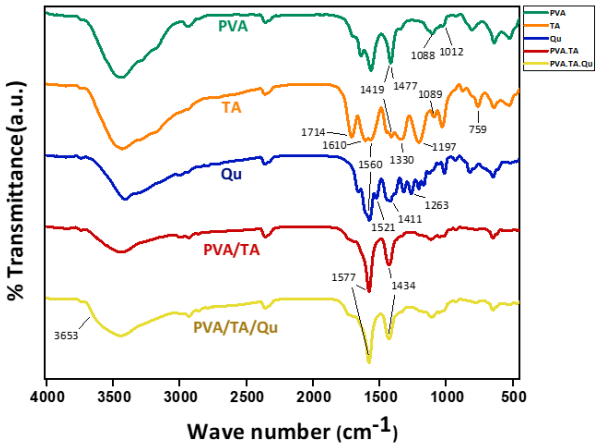
Today, cancer is considered as a serious disease threatening public health around the world. Surgery is often used as a primary treatment for removing tumor cells, but there is still a risk of recurrence of the disease due to remaining cancer cells after surgery. One of a drug delivery systems in cancer treatment after surgery is the placement of implants made of biocompatible materials. In this study, a multifunctional hydrogel is formed using natural and synthetic materials containing Polyvinyl alcohol and Tannic acid(TA) to prevent cancer recurrence. It is possible to load drugs such as quercetin(Qu) ,as a new anti-cancer compound, in it. TA and Qu both have properties such as antioxidant, antibacterial, coagulation and anti-inflammatory effects. On the other hand The use of hydrogels due to these unique properties such as high biocompatibility, slow release of drugs and other therapeutic agents is is one of the best ways to prepare implants.

Materials and Methods

Four types of hydrogel with different concentrations of TA were made and they were evaluated for physicochemical properties, yield percentage, initial water content, composed gel content, swelling percentage, water retention capacity, release profile of tannic acid and quercetin from hydrogel, biodegradability percentage in-vitro conditions and blood compatibility of hydrogel. then the optimum concentration of TA was selected and after loading the drug, X-ray diffraction (XRD) tests, Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetric (DSC) analysis were performed for the hydrogels and their raw materials.

Results and Discussion

The results showed that by changing the concentration of TA, the physicochemical properties of hydrogel can be easily changed. the results of FTIR, XRD and DSC tests confirmed the formation of hydrogel and drug loading inside the hydrogel. Hydrogel showed controlled and pH-dependent release for Tannic acid and Quercetin.



FTIR Diagram of PVA, TA, Qu, PVA/TA, PVA/TA/Qu

Conclusions

The results show that due to the properties of flexibility, low toxicity, excellent biocompatibility of these hydrogels and utilization of inherent anti-cancer properties and wound healing properties of Tannic acid and Quercetin, this hydrogel can be placed in the tumor site after surgery in order to prevent cancer recurrence and improve the wound healing process.

Keywords

Cancer, Hydrogel, Polyvinyl alcohol, Tannic acid, Quercetin

References

1.Aquib M, Juthi AZ, Farooq MA, Ali MG, Janabi AHW, Bavi S, et al. Advances in local and systemic drug delivery systems for post-surgical cancer treatment. Journal of Materials Chemistry B. 2020;8(37):8507-18.
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Formulation and evaluation of omeprazole-Chitosan microparticles coated with Eudragit prepared by spray drying for making suspension

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Introduction

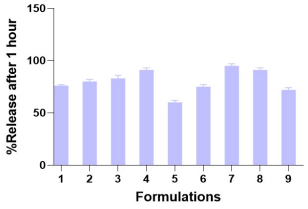
Omeprazole is administered in gastric hypersecretion-associated disorders, but a liquid pediatric formulation is not available in our community due to chemical instability of the base in acidic conditions. Here, spray drying was utilized to process omeprazole microspheres for further reconstitution of the powder in water with enhanced stability [1]. Carboxymethyl Chitosan (CMC) and Eudragit S100 (ES100) were employed to act as mucoadhesive and acid protective agents, respectively [2].

Materials and Methods

The feed solutions containing omeprazole, CMC, and ES100, at different ratios, were prepared and spray-dried under constant condition of 110◦C inlet temperature, 70% aspiration and flow rate of 5mL/minute. Yield of process, encapsulation efficiency (EE) as well as release profile were quantified in different powders. Design-Expert 13 software was engaged to screen and analyze the responses and further select the sample with most desirable properties. All experiments were done in triplicate.

Results and Discussion

The employed weight ratios of CMC to omeprazole varied from 0.5 to 5 with concomitant presence of ES100 from 0.5 to 10. Analysis of dependent responses demonstrated the ranges varied from .... to .....% for yield, 85 to 111 % for EE, 60 to 95% for release in neutral condition within 1 hour, respectively, Figure 1. The optimum level of ES100 was required to provide the best dissolution performance since the higher amounts created a thick layer around the microspheres while the lower amounts make them vulnerable to acid. CMC could suitably protect omeprazole from degradation within the process, but higher amounts might limit the drug release.



Samples	CMC	ES 100
F1	2.75	11.9
F2	0.5	10
F3	0	5.25
F4	5	10
F5	5	0.5
F6	5.9	5.25
F7	2.75	5.25
F8	0.5	0.5
F9	2.75	0

Conclusions

The results of the current study demonstrated promising perspective for preparation of spray-dried microspheres of omeprazole in the presence of CMC and ES100 at suitable ratios. Further evaluations should be done to assess the efficacy of the powders via in vivo models as well.

Keywords

Omeprazole; Chitosan; Eudragit S100; Spray drying; Release

References

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Fabrication of a dissolvable photothermal polymeric microneedle containing bismuth nanoparticles for cancer therapy

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Introduction

Skin cancer is one of every three cancers diagnosed and it can be divided into melanoma and non-melanoma [1]. Since these lesions appear more on the surface of the skin, it is so favorable to have an effective treatment system for topical drug delivery and minimizing the systemic distribution. In the current work, we use microneedle-mediated combination therapy to treat melanoma. For this purpose, sorafenib (SFN), a multi-kinase inhibitor was selected for chemotherapy [2] and bismuth sulfide (Bi2S3) nanoparticles (NPs) with photothermal activity were used for photothermal therapy, both incorporated in a microneedle (MN) made by polyvinylpyrrolidone (PVP), a biocompatible water-soluble polymer. The prepared MN patch, called PVP-Bi2S3-SFN, was prepared and its therapeutic effects were investigated.

Materials and Methods

For the Bi2S3 NPs preparation, thioacetamide (TAA) was dissolved in deionized water (DIW) under vigorous stirring and the prepared solution was added to ethanol 96% (v/v) and DIW. In the next step, Bi (NO3)3 · 5H2O was dissolved in DIW/glycerol 85% (v/v) (1:1) under stirring and then was added to the above solution under constant stir. The prepared NPs and SFN were loaded into PVP 20%, and then the made solution was poured by a solvent-casting method onto a PDMS mold followed by centrifugation at 4500 rpm for 20 min to fill the MN cavities. Subsequently, PVP (17% w/v) was added into the tip-embedded PDMS mold, centrifuged, and left to dry in a desiccator. Eventually, the MN patch was carefully peeled off after overnight drying.

Results and Discussion

The FTIR, TGA, XRD, and EDAX results showed that the synthesis of Bi2S3 NPs was successful. As shown in Figure 1A, Brunauer–Emmett–Teller (BET) analysis proved the pore volume and mean pore diameter of the nanoparticles are 0.2791 cm3 g-1 and 43.36 nm, respectively. Also, according to the microscopic images and SEM, the obtained needles are about 650 µm in height and 290 µm in width (Figure 1B). According to the mechanical test data, the prepared patch has sufficient ability to penetrate the skin and deliver the drug (Figure 1C). Considering the dissolution rate on the surface of mice skin, the results showed that the time required for the needles to dissolve sufficiently is about 20 minutes (Figure 1D), and the materials used to prepare the fine needles are non-toxic and completely biocompatible (Figure 1E). In addition, the in vitro, and in vivo photothermal testing exhibited that the nanoparticles have the ability to raise the temperature adequately to kill the tumor (Figure 1F).

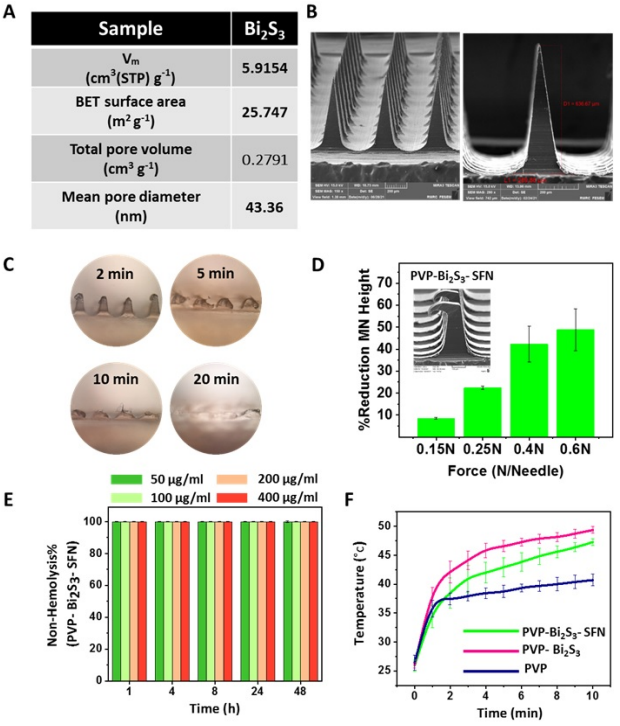

Figure 1 A)BET analysis data of the synthesis NP. B)SEM images of fabricated MNs. C)Microscopic images of in vivo dissolution rate. D)The mechanical behavior of the needles. E)In vitro hemolysis results. F)In vivo photothermal properties measurement.

Conclusions

We demonstrated the fabricated polymeric MN patches have desirable physicochemical properties with enough mechanical strength for skin insertion and biocompatibility. Further, the encapsulated nanoparticles displayed applicable photothermal ability to destroy the tumor cells. Nevertheless, verification of combination therapy capacity of prepared MNs against skin cancer in vivo analysis is also required which is ongoing.

Keywords

Melanoma, Microneedle, Combination therapy, Bismuth nanoparticles, Photothermal therapy

References

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Formulation and Processing of Dry Powders of Trastuzumab via Spray Freeze Drying and Evaluation of Physicochemical Properties and Stability

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Introduction

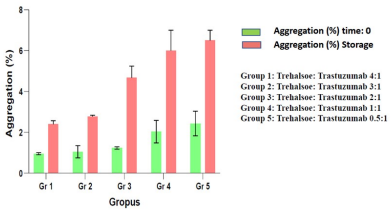
Monoclonal antibodies are highly recommended for the treatment of various disorders, but they are prone to physicochemical instabilities in the liquid state. Drying technologies can enhance their stability such as spray freeze drying (SFD). Trastuzumab as one of the top-selling products is used in breast and specific type of the lung cancers [1]. The latter application proposes the logic for topical lung delivery of the drug for reducing the dose and adverse reactions. Here, SFD was employed to process stable dried powder for further respiratory delivery of trastuzumab.

Materials and Methods

The antibody was formulated with various ratios of trehalose, sprayed under liquid N2 and transferred to freeze dryer (-50º and 25ºC, 24 hours, 0.01 mBar). Size exclusion chromatography detected aggregation or fragmentation after preparation and 6 months of storage at 45ºC. Conformation and thermal behavior were analyzed by fourier-transform infrared spectroscopy and differential scanning calorimetry, respectively. Twin stage impinger was used to evaluate in vitro powder aerosolization. All tests were done in triplicate.

Results and Discussion

The best ratio of antibody to trehalose was 1:3 which provided the aggregation (1.05 and 2.76% after process and storage, respectively) with no fragments, but the highest fine particle fraction (FPF) of 51%. The confirmation of amorphous powders was well-preserved. Higher ratios of trehalose provided more hydrogen bonds with antibody in the absence of water which protected the product against aggregation [2]. Although the ratio of 1:4 antibody to trehalose caused the least aggregation, Figure 1, the FPF was significantly lower than the ratio of 1:3 due to hygroscopic nature of trehalose which adversely influence aerodynamic behavior of the powder.



The profile of aggregation (%) after process and storage in prepared formulations.

Conclusions

Spray freeze drying can be used as a method of choice to process dried powder of trastuzumab with enhanced stability. Further studies should be done to confirm the in vitro and in vivo efficacy of the powder as well.

Keywords

Trastuzumab; Spray freeze drying; Trehalose; Chromatography; Stability.

References

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Preparation and characterization of chitosan hydrogel loaded by ZnO nanoparticle and Vancomycin: Potential carrier in antimicrobial therapy

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Introduction

Infectious disease has always a contrary effect to human beings as it is a pathological situation. Antibiotics are one of the most effective and useful compounds in the fight against various types of infections, but the main problem is resistance to antibiotics. One of the most widely used drug options among antibiotics is vancomycin. Zinc oxide nanoparticles have shown good efficiency against antibiotic resistance bacteria. On the other hand, hydrogel as a drug delivery system can make long term release of drug within therapeutic range. In this study, ZnO nanoparticles synthetized and loaded with vancomycin into chitosan hydrogel prepared by 2% w/w of genipin as cross linker. ZnO nanoparticles characterized by XRD analysis and prepared hydrogels was characterized by FESEM and evaluated its swelling ratio and release profile in different pH.

Materials and Methods

ZnO nanoparticle was synthetized and characterized by XRD and FESEM microscopy. Then chitosan hydrogel prepared by 2% w/w of genipin as cross linker and after preparation of hydrogel, 100 mg vancomycin was loaded into the chitosan hydrogel along 10 mg ZnO NPs. The obtained hydrogels were characterized by different methods including FESEM, FTIR, swelling ratio assessment and release study in different pHs.

Results and Discussion

XRD rseults demonstarted ZnO nanoparticles was synthetized with crystallin size 40.98 nm. FESEM of prepared chiotsan hydrogels showed hydrogel structure and FTIR results demonstarted synthesis of chitosan hydrogel by genipin crosslinker. The swelling ration in different pHs showed chitosan hydrogel has higher swelling in pH 5.8 in compared with pH 7.4. Furthermore, the release profile showed the release of vanocmyin can be increased in repsonse to acidic pH up to 80% in 4 days which show formulated hydrogel can response to infected media by increasing drug release.

Conclusions

In conclusion, findings of present study showed that designed chitosan hydrogel can be a potential antimicrobial pH responsive carrier to sustain releasing antibiotics and overcome microbial resistance in infection diseases.

Keywords

Chitosan, Hydrogel, Nanoparticle, vancomycin

References

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(3) Oustadi F, Imani R, Haghbin Nazarpak M, Sharifi AMJPfAT. Genipin-crosslinked gelatin hydrogel incorporated with PLLA-nanocylinders as a bone scaffold: synthesis, characterization, and mechanical properties evaluation. 2020;31(8):1783-92.

Preparation and evaluation of chitosan/aloe vera gel loaded by ZnO nanoparticles for wound healing

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Introduction

Topical treatment for wound healing is preferable because it is less toxic and has a faster effect. Aloe vera gel has strong immunomodulatory activity and it can inhibit the inflammatory process following wound injury. Chitosan is a natural biopolymer which shows considerable properties in medical field, such as hemostasis, wound healing, bacteriostatic, biocompatibility and biodegradability properties. Studies have shown that chitosan have no adverse effects after implantation in tissues for using as an effective agent to inhibit fibroplasia in wound healing. Zinc oxide nanoparticles (ZnO) can interact with bacterial surface where it enters inside the cell, and subsequently exhibits bactericidal mechanisms and therefore cause to decreaing the time of wound helaing. Therefore, It seems preparation of chitosan / aloe vera gel loaded by ZnO NPs as a novel formulation which is the in aim of this could be considered as a potential hope for effective wound healing.

Materials and Methods

ZnO NPs were synthesized and characterized by XRD and FESEM microscopy. The chitosan and aloe vera gel were prepared by dissolving chitosan in acetic acid and obtaining chitosan gel 2 % w/v then aloe vera powder was added to chitosan gel with different ratio 1:1 and 2:1 chitosan to aloe vera. After 24 hours the ZnO NPs (1 mg/ml) was added to prepared gels and then 24 hours stirred at 37ºC. The obtained gels were characterized in the regard of viscosity, gel consistency and pH

Results and Discussion

The ZnO NPs was characterized and XRD results showed crystalline size of ZnO nanoparticles was 31.8 nm. The FESEM results showed the synthetized nanoparticles are rod shape with mean diameter size 33.27 nm. The formulated chitosan/ aloe vera gel had pH 4.5 and both formulations showed good gel consistency and skin spreadability. It seems both chitosan / aloe vera ratio could be acceptable for more investigation in vivo

Conclusions

In conclusion, the prepared chitosan / aloe vera gel loaded by ZnO NPs can be a potential wound healing topical formulation with good consistency

Keywords

Aloe vera, Chitosan, Zinc, Nanoparticle

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Minoxidil-loaded methylated aminobenzyl carboxymethyl chitosan nanoparticles: Physicochemical characterization

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Introduction

Androgenic Alopecia (AA) is the main cause of hair loss in both sexes. Minoxidil (MX) is known to have an effect on the anagenic phase of hair cycle by promoting hair growth and is considered as a topical treatment of AA. In order to enhance the solubility of MX and also its penetration into the hair follicles, co-solvents like ethanol and propylene glycol, are routinely used. These co-solvents are the main cause of irritation and allergic contact dermititis related to the formulations available on the market. Nano based drug delivery systems are used to enhance the solubility of lipophilic molecules and thus maximize the concentration of the drug in the hair follicles. Chitosan (CS) is commonly used in the medical field because of its biodegradability and biocompatibility. Methylated Aminobenzyl Caboxymethyl chitosan (MCS), a derivative of chitosan, is an amphiphilic molecule. The amphiphilicity of this polymer can mediate a major impact on the drug loading and penetration of MX.

Materials and Methods

CS and MCS nanoparticles containing MX were prepared by Ionic Gelation method. The optimum formulations were selected based on the amount of drug loading and then followed by the analysis of their physicochemical properties including particle size and Zeta Potential.

Results and Discussion

The formulation of CS nanoparticles with the ratio of chitosan to TPP 11:1 loaded with 10 mg of MX and the formulation of MCS nanoparticles with the ratio of 7:1 chitosan to TPP loaded with 2.4 mg of MX were selected as the optimum formulations. CS nanoparticles have reached a drug loading of 93% and showed particle sizes of 101 nm with a Zeta Potential of +17 mV. In the other hand, MCS nanoparticles successfully attained a drug loading of 92% and demonstrated particle sizes of 224 nm with a Zeta Potential of +10 mV.

Conclusions

Considering the fact that the amount of drug loaded in MCS nanoparticles is less than in CS nanoparticles, a similar efficiency associated to the upcoming skin permeation tests and animal study results for both formulations can further confirm the advantages regarding the MCS nanoparticles and it can thus, approve the potential properties that MCS can bring into improving the current formulations for the treatment of AA.

Keywords

Nanoparticles, Minoxidil, Chitosan, Chitosan Derivative

References

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A Multifunctional Photoactive Hydrogel Containing Bismuth Sulfide Nanoparticles for Synergic Photo-Chemo-Immunotherapy of Cancer

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Introduction

Cancer is the second leading cause of mortality worldwide. Unfortunately, there are currently no fully satisfactory approaches to treat cancer, and options are mainly limited to chemotherapy, radiotherapy, immunotherapy, and surgery, are not specifically directed to tumor cells, and may also affect healthy tissue. Photothermal therapy (PTT) has attracted extensive attention in cancer therapy owing to the minimal damage to non-target tissues. Bismuth Sulfide nanoparticles are promising photothermal agents for cancer therapy due to their light-to-heat conversion ability to induce apoptosis in tumor cells [1]. The combination of PTT with chemotherapy and immunotherapy has a high potential to increase the chance of cancer eradication without metastasis to other vital organs [2]. In this work, cancer cell-membrane (CCM) and sorafenib (SFN) were loaded into a photoactive injectable hydrogel to render tumor-specific immunotherapeutic function and chemotherapy to the prepared hydrogel [3].

Materials and Methods

Bismuth Sulfide nanorods (NRs) were prepared using a simple chemical reaction and coated with hyaluronic acid to form BiH NRs. An injectable hydrogel of poly methyl vinyl ether-maleic acid (PMVE-MA) and gelatin was prepared via chemical crosslinking. BiH NRs, CCM, and SFN, were loaded within the hydrogel. The physicochemical characterization and photothermal performance of the NRs and hydrogels were assessed. Afterward, the hemocompatibility, the in vivo toxicity, the in vitro and in vivo antibacterial activity of the hydrogels, and its anti-cancer effect were evaluated on a 4T1 tumor-bearing mouse model.

Results and Discussion

The rod shape nanoparticles, with an average particle size of about 57 nm were successfully loaded into the chemically crosslinked hydrogel. The viscosities of hydrogels decrease with increasing shear rates in different time points, indicating the shear-thinning behavior of hydrogels. In addition, the force required for injection of the hydrogel 3 h after preparation was about 41 N using a 21 G syringe, which confirms the injectability of the hydrogels. BiH-loaded hydrogel demonstrated sufficient temperature elevation to kill cancer cells after 10 min of near-infrared (NIR) irradiation. The hematoxylin and eosin staining of the main organs of treated rats showed no significant histopathological changes in the main organs. In addition, the BiH-loaded hydrogel showed very potent antibacterial activity with and without NIR irradiation. The combined intratumoral photo-chemo-immunotherapy demonstrated more anticancer effect than the individual photo-, chemo- or immunotherapy alone.

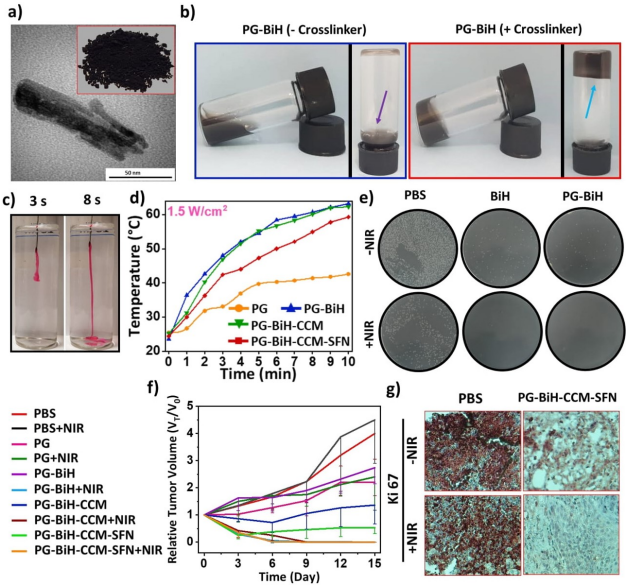

Figure 1. a) TEM of BiH, b) Photographic images of the PG-BiH with or without crosslinker at 70°C. c) Injectability, d) Photothermal effect of hydrogels, e) Antibacterial effect against S. aureus, f,g) Anticancer effect.

Conclusions

In this study, an injectable hydrogel containing BiH NRs, CCM, and sorafenib for photothermal therapy against cancer was reported, which shows excellent photo-heat conversion ability of BiH NRs, and the synergistic effect of using a combination of chemotherapy, photothermal therapy, and immunotherapy was evaluated in this study. In addition, the injectable hydrogel had the capability to load drugs for sustained release at the cancer tissues over a long period.

Keywords

Injectable Hydrogel, Photothermal therapy, Chemotherapy, Immunotherapy, Breast Cancer

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Preparation and evaluation of berberine-phospholipid complex to improve its dissolution properties

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Introduction

Berberine, an alkaloid constituent of the Barberry (Berberis vulgaris L.), is present in the roots, rhizomes, stem, and bark of B. vulgaris and many other plants. Berberine has several pharmacological effects including antimicrobial, anti-diabetic and anti-cancer. Berberine has low oral bioavailability due to poor aqueous solubility and insufficient dissolution rate, which can reduce its efficacy upon orall administration. This study aimed to develop and characterize berberine-phosphatidylcholine complex (BPC) to enhance solubility and oral bioavailability of berberine.

Materials and Methods

BPC with different molar ratio of berberine-phosphatidylcholine (1:1, 1:2, 1:3) was prepared by the solvent evaporation method and their physicochemical characteristics were investigated by fourier transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR), differential scanning calorimetry (DSC), X-ray diffraction (XRD). Berberine content of BPC as well as its water solubility and in vitro dissolution rate were evaluated.

Results and Discussion

Berberine: phosphatidylcholine with 1:2 molar ratio showed the best complexation with the highest water solubility and was selected as the optimal ratio of BPC. The BPC dissolution rate also increased in the simulated intestinal medium. It can be concluded that due to the phosphatidylcholine content, berberine dissolution could be improved by the formation of micelles.

Conclusions

It is concluded that the phosphatidylcholine association of berberine may be considered as a potential technique for improving the berberine solubility and hence its bioavailability.

Keywords

Berberine, Phospholipid, bioavailability improvement, dissolution improvement

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lipid nanoparticles as a potential tool to overcome antimicrobial resistance

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Introduction

Over the preceding decade, solid lipid nanoparticles have emerged as an innovator of the continuously developing field of nanotechnology with several potential applications in drug delivery systems, clinical medicine and research. Mupirocin is known as an antibacterial agent produced by pseudomonic acid A. Despite its unique structure and mechanism of action standing from other antibiotics, mupirocin significantly affects Staphylococcus aureus (S. aureus). The purpose of the current research was to formulate mupirocin in solid lipid nanoparticles (SLNs) to enhance physicochemical properties, control drug release, and antibacterial effect to decrease antibiotic resistance.

Materials and Methods

Mupirocin-loaded SLNs were prepared by a modified micro emulsion-based method. Particle size, zeta potential, polydispersity index (PDI), drug loading and encapsulation efficiency of the formulations were calculated. Transmission Electron Microscopy (TEM) and X-ray powder diffraction (XRD) were used to assess the crystalline properties of drug-loaded SLNs. In vitro release profile of formulation was tested using a dialysis bag in water-ethanol 96% with 100:2 ratio. Moreover, the conventional Broth Macrodilution tube and Agar Well Diffusion were used to determine antibacterial activity of mupirocin-loaded SLNs against S.aureus.

Results and Discussion

Results showed that encapsulation efficiency, drug loading, size and zeta potential were measured 92/5, 8/4%, 31/69 nm, -24/7 mv respectively. The crystallinity index was 72%. The resulting SLNs were spherical with a diameter of 20 nm. The formulation also sustained the drug release for 24 hours without any primary burst effect. The minimum inhibitory concentration (MIC) of drug-loaded SLNs was two times less than the free drugs.

Conclusions

According to the physicochemical properties, the formulation has high encapsulation efficiency with adequate particle size and desirable zeta potential (stability). From the prolonged-release profile of formulation, it can be determined that mupirocin-loaded SLNs will decrease the administration frequency. The MIC of mupirocin-loaded SLNs was two times more effective than the mupirocin solution against S.aureus. Consequently, it could be concluded that mupirocin might have more antibacterial efficacy by delivering as SLNs against S.aureus to decrease antibiotic resistance.

Keywords

Solid lipid nanoparticles, Mupirocin, Antibacterial, Staphylococcus aureus ,Drug Delivery

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A Hemostatic Injectable Photothermally-Active Hydrogel Prepared via Metal-Coordinated Crosslink for Wound Healing and Cancer Therapy

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Introduction

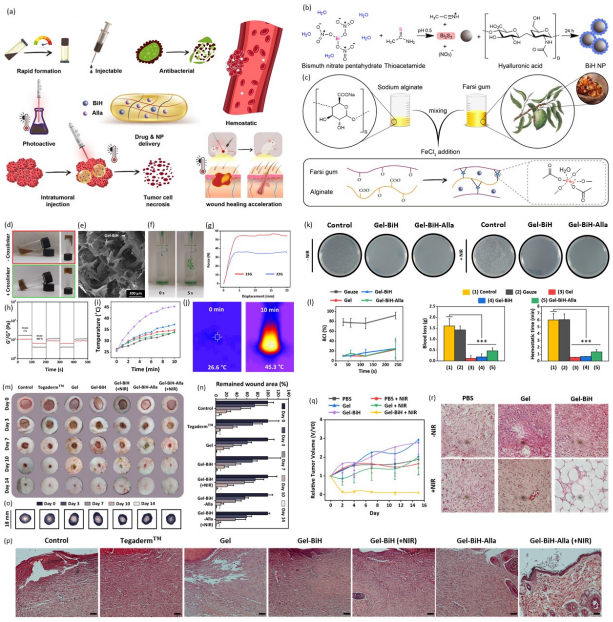
Photothermal therapy (PTT), a promising noninvasive strategy, has intrigued emerging attention due to its widespread clinical applications. Also, activities to prevent the occurrence of second cancer like surgery and radiation therapy cause several side effects, affecting the overall health of patients[1]. Herein, we reported a PTT-assisted antibacterial system utilizing bismuth sulfide nanoparticles (BiH NPs) and allantoin (Alla) as a hydrophilic drug farsi gum-alginate hydrogel. So the aim of this study is to use photothermal therapy as a local treatment strategy with minimal toxicity and high specificity in tumor cells is a promising approach for cancer ablation and wound healing acceleration (Fig. 1a)[2].

Materials and Methods

BiH NP synthesis was carried out (Fig. 1b) and Gel-BiH-Alla hydrogel was prepared through abundant metal coordinated bonds among the functional groups of farsi gum and alginate via ferric ions (Fig. 1c). Physicochemical characterizations were performed to confirm the formation of the hydrogel and injectability, rheology properties, and photothermal effect of hydrogels were assessed. Moreover, antibacterial activity and blood clotting tests were evaluated. Subsequently, in vivo wound healing and cancer phototherapy evaluations were carried out.

Results and Discussion

The rod-shaped NPs, were synthesized and successfully loaded in the hydrogel. Gel formation assessment of hydrogel was proved (Fig. 1d) and scanning electron microscopy (SEM) results confirmed the porous structure of the hydrogel (Fig. 1e). In addition, the prepared hydrogel showed desirable injectability, self-healing, and photothermal performance (Fig. 1f-j). Also, the hydrogel showed essential antibacterial activity (Fig. 1k) and the blood clotting test showed a significant decrease in hemostatic time and blood loss in hydrogel-treated groups in comparison to the control groups (Fig. 1l). In vivo wound healing study and hematoxylin and eosin (H&E) staining demonstrated that wound area in Gel-BiH-Alla + NIR was the most efficient group in wound closure (Fig. 1m-p). Also, In vivo cancer phototherapy and related H&E staining results showed the relative tumor volume decreased and apoptotic cells presence in just Gel-BiH + NIR (Fig. 1q,r).



a-c) The schematic illustration of BiH synthesis and hydrogel preparation. d-j) Physicochemical studies. k, l) Antibacterial and hemostatic performance. m-r) Wound healing and cancer therapy functions.

Conclusions

This novel multifunctional hydrogel demonstrated excellent hemostatic, antimicrobial, and photothermal-induced skin regeneration performance, leading to great application potential in wound healing and cancer therapy.

Keywords

Multifunctional Biomaterials, Photothermal Therapy, Injectable Hydrogels, Cancer Thermotherapy, Wound Healing

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Photothermally Active pH-Responsive Polydopamine@ MnO2 Nano-platform Encapsulated into Platelet Cell Membrane for Multifunctional Cancer Ablation

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Introduction

Cancer is a worldwide challenge[1]. Traditional cancer therapies suffer from systemic toxicity, off-target drug leakage, rapid clearance, and poor selectivity, all resulting in undesirable therapeutic performance. Photothermal (PT) therapy as a novel approach in cancer treatment[2], when combined with chemodynamic therapy, and active targeting can eradicate tumor tissue via hyperthermia by harvesting near-infrared (NIR) light, reactive oxygen species (ROS) generation, and on-demand drug release at the tumor site[3]. Polydopamine nanoparticles (PDA NPs) with high light absorption in the NIR region as PT agents kill cancer cells by thermal effect. MnO2 shell with pore capping property covers the mesoporous structure of PDA core and prevents premature release of loaded drug and triggers cell death reactions by generating ROS under NIR irradiation. Platelet cell membrane (PCM) cloaked PDA@MnO2 NPs provide actively targeted systems by targeting over-expressed CD44 receptors of cancer cells.

Materials and Methods

Dopamine hydrochloride (DA-HCl), pluronic® F-127, and potassium permanganate (KMnO4) powder, 3, 3′, 5, 5′-Tetramethylbenzidine (TMB) and Ammonia (NH3) solution were purchased from Sigma-Aldrich. Platelet-rich plasma (PRP) was provided by Zanjan Blood Transfusion Organization. To synthesize PDA NPs, 0.15 g of DA-HCl and 0.1 g of Pluronic® F-127 were added into 10 ml of deionized water (DW)/ ethanol. After complete dispersing, 160 µL TMB was added and the solution was sonicated for 2 min. After adding 375 µL NH3 dropwise, the solution was stirred to complete the reaction for 2 h. finally, PDA NPs were centrifuged and washed with DW and 70% ethanol. Next, PDA dispersion was sonicated and 4 mL KMnO4 solution was added dropwise. The solution was stirred for 24 h to obtain PDA-MnO2 NPs after centrifugation and washing processes. Also, PCM was extracted from the platelet through 4 freeze-thaw cycles, added into 1 mg/mL of PDA-MnO2 NPs, and sonicated for 3 min to obtain PDA-MnO2@PCM NPs.

Results and Discussion

PDA NPs can efficiently absorb NIR light, and convert it into the fatal heat at the location of cancer cells. The maximum temperature of PDA-MnO2@PCM NPs (100 µg/mL) in aqueous solution was increased to 57.4 ˚C under the NIR laser (1.5 W/cm2) irradiation for 10 min. Meanwhile, the required temperature to induce ablation of cancer cells is 43.0 ˚C. By increasing the power density of NIR light, the recorded temperatures of all tested NPs at the constant concentration (200 µg. mL-1), were increased. Also, there is a positive and direct relationship between the laser's power density, the concentration of the prepared NPs, and recorded temperatures. The heat-to-light conversion efficiency of PDA-MnO2@PCM NPs was calculated to be 52%. Also, the photothermal properties of PDA-MnO2@PCM NPs during five ON/OFF cycles of NIR laser irradiation follow a constant trend, demonstrating their desirable photostability.

Photothermal performance assessment of PDA, PDA-MnO2, PDA-MnO2@PCM NPs.

Conclusions

In conclusion, we have designed and fabricated an innovative nanoplatform based on PDA-MnO2@PCM NPs to demonstrate both site-targeted photothermal and chemodynamic therapeutic effects for cancer treatment. It was found that the PDA-MnO2@PCM NPs have excellent photothermal performance under NIR laser irradiation. Also, the results showed the potential of loading chemotherapeutic agents and synergistic photo/chemotherapy of cancerous cells. pH/NIR laser-triggered release manner could prove cancer site-specificity of drug accumulation. Finally, our research has highlighted the importance of designing innovative nanosystems to change the landscape of cancer treatment.

Keywords

Photothermal therapy, Nanoparticle, Cancer, Platelet cell membrane, Active targeting

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Prediction of the IC50 of pyridine crystal Materials on the Basis of their Molecular Structures: Novel architecting for anti-cancer drugs

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Introduction

In cancer therapies, cancer cells have to be declined or removed. Enough concentration of drugs has an effective inhibitory influence on cells is defined with IC50. This study investigated the Quantitative structure-activity relationship (QSAR) of 17 anti-cancer crystal compounds [1,2] based on pyridine on Hela cells with Multiple Linear Regression (MLR). This computational model can predict the biological properties of compounds before examining experimental tests.

Materials and Methods

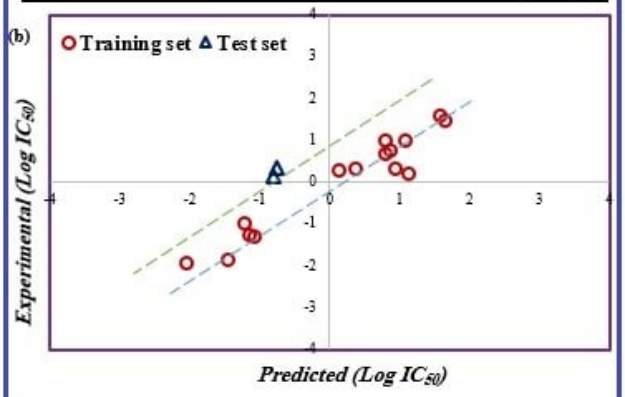
The collected structures with their IC50 (https://uupload.ir/view/ic505_m6z9.docx/) are demonstrated in Figure 1a. The Hyperchem software was used to optimize the compounds. Then the best configurations were extracted by Dragon for analyzing the molecular descriptors. The SPSS software was used for the statistic computations and other computational methods [2,3].

Results and Discussion

In this research, 15 compounds were selected randomly as training sets and two as test sets for new modeling. The values of independent descriptors were utilized for computing IC50. After estimating, the descriptors were depicted as nRNR2 for the number of tertiary amines (aliphatic), MATS4m for Moran autocorrelation of lag 4 weighted by mass, and E1v for 1st component accessibility directional WHIM index/weighted by van der Waals volume. According to the equation, the Elv descriptor makes the IC50 more negative, significantly influencing this parameter. The results illustrated that R2 and MSE were 0.968 and 0.05 in the training test, respectively, although these parameters were subsequently 1.00 and 0.01 in the test set Figures 1b,c.

$$Log\ IC50 = 2.456–1.095\times nRNR2+5.436\times MATS4m–2.878\times E1v$$

(a)	IC_{50}	Exp. Log IC_{50}	Pred. Log IC_{50}	Dev.	CCDC No.
Training set					
1.	0.035	-1.460	-1.850	0.394	[718696]
2.	1.340	0.130	0.297	-0.169	[776692]
3.	36.000	1.560	1.591	-0.034	[869871]
4.	43.000	1.630	1.496	0.137	[869872]
5.	6.000	0.780	1.032	-0.254	[1006028]
6.	11.770	1.070	0.997	0.074	[1823137]
7.	0.009	-2.050	-1.906	-0.140	[1829047]
8.	0.080	-1.100	-1.293	0.196	[1829048]
9.	0.070	-1.150	-1.238	0.083	[1829046]
10.	2.290	0.360	0.323	0.037	[1574994]
11.	8.510	0.930	0.338	0.591	[1574995]
12.	6.090	0.780	0.687	0.098	[1000145]
13.	7.300	0.860	0.778	0.085	[700683]
14.	0.058	-1.240	-0.973	0.177	[718694]
15.	13.280	1.120	0.226	-0.071	[1406755]
Test set					
16.	0.160	-0.800	-0.767	-0.028	[1406752]
17.	1.430	0.160	0.325	-0.170	[1406754]



(C)	Model	Sets	R^2	MSE	Q^2
	$logIC_{50}$=2.456–1.095×nRNR2+5.436×MATS4m–2.878×E1v	Training set	0.968	0.050	0.918
		Test set	1.000	0.010	1.000

Figure 1. a: Training and test sets , b: Experimental versus predicted values diagram, c: Statistical parameters.

Conclusions

According to QSAR results, a novel, simple MLR model can be used for other similar compounds. This work was satisfying and robust for developing a future view of the anticancer carrier and suitable compounds.

Keywords

QSAR, MLR, IC50, Pyridine

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Development of a novel solid lipid nanoparticle-based system for enhanced in vivo topical anti-inflammatory activity

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Introduction

Hesperidin, a flavone glycoside abundantly present in citrus fruits, has proven therapeutic activities including anti-inflammatory effect [1]. Some micro and nano systems have been developed for efficient delivery. Another benefit is controlled release of therapeutic agents. Among the novel delivery systems, lipid nanoparticles are preferred for skin delivery of pharmaceutical agents due to safe interactions and similarity to structure of stratum corneum. Solid lipid nanoparticles (SLNs) provide additional attributes such as controlled release and targeted drug delivery. Herein, we report a novel formulation of HESP loaded solid lipid nanoparticles [3].

Materials and Methods

SLNs were prepared using hot homogenization and ultrasound method. The formulation was developed and optimized by response surface method, and characterized by TEM, FT-IR, and DLS. Encapsulation efficiency was determined and the anti-inflammatory effect was assessed through in vivo model. Drug release was performed by Franz Diffusion Cell method in mouse skin [3].

Results and Discussion

The optimum formulation was selected with small size of 179.8 ± 3.6 nm, and with high encapsulation efficiency (93.0 ± 3.8 %). Morphological tests showed spherical shape. The absence of HESP peak could be ascribed to the dispersion of amorphous drug into lipid matrix of SLNs. HESP-SLNs formulation presented a stronger anti-inflammatory response than either HESP cream and HESP free SLNs. The application of HESP-SLNs and indomethacin significantly decreased the inflammation in comparison with xylene treated group. No significant differences were found between HESP-SLNs and indomethacin effects. The in vitro permeation studies exhibited that HESP-SLNs could significantly enhance cutaneous uptake of HESP and skin targeting[2].

Conclusions

The outcomes exhibited that encapsulation of HESP in SLN carrier improves the anti-inflammatory potential of this natural agent.

Keywords
Solid lipid nanoparticle; Hesperidin; Anti-inflammatory; Response surface method; Ear edema.

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Synthesis and Characteristic of Trimethyl Chitosan nanoparticles coated with polyelectrolyte for RNAi delivery.

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Introduction

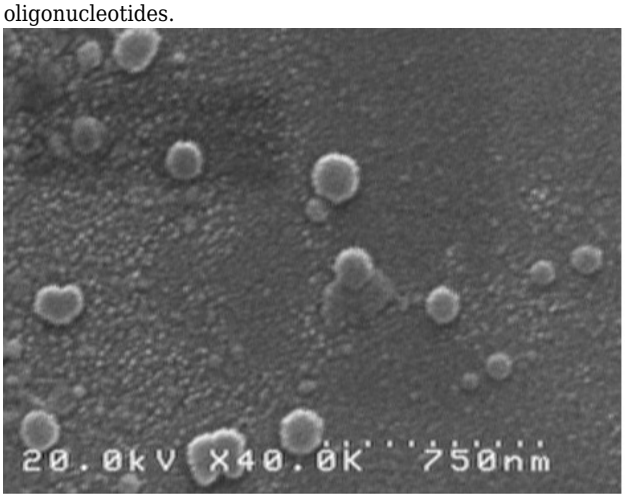
RNA interference, has been rapidly expand among cancer researches due to its high specificity and efficacy. However, safe and effective delivery of RNAi to the specific targets faces lots of challenges according to its instability, hydrophilicity and large molecular weight [1]. Despite ongoing researches, developing suitable carriers for gene deliver and gene therapy is still challenging. Nanodelivery systems based on cationic polymers such as Trimethtly chitosan (TMC) are able to highly encapsulated genes and facilitated cellular uptakes by interaction with the negative charge of the cell surface [1-2]. The negatively charged polyelectrolytes could be used in order to form nanoparticles. Also, several cancer cell line express the CD44-receptors on their surface, consequently it seems that Hyaluronic acid (HA) is a noteworthy component for gene delivery to cancer cells.

Materials and Methods

Low molecular weight chitosan (100-150 kDa), and Hyaluronic acid (MW=25046 Da) were purchased from Sigma. siRNA was purchased from BIONEER Korea. Trimethyl chitosan synthesized and its structure was characterized using HNMR spectroscopy. Active-targeted Hyaluronic acid recoated TMC nanoparticles was generated by ionic gelation method. The size, zeta potential, and polydispersity index of nanoparticles were assigned by dynamic light scattering and the surface morphology and size of nanoparticles were observed using scanning electron microscopy. For measuring the loading efficiency, the best N/P of siRNA/NPs were measured by agarose gel electrophoresis.

Results and Discussion

Optimum nanoparticles had the following characteristics: Hydrodynamic size ~160 nm, PDI~0.2 and Zeta potential ~ +19. SEM image represents the regular globular nanoparticles. The estimated size of SEM results was smaller than DLS data. Briefly, 1.2, 2.5, 5, 10, 20, 30, 40 and 50 µg of siRNA was applied to load into NPs. HA-TMC NPs could encapsulate up to 50 µg siRNA. Since RNA molecules are known to be easily degraded in bloodstream, several carriers have been designed and utilized to protect and improve its bioavailability and biological effects. Highly pH dependent solubility of chitosan may result in its instability in physiological pH. To address these issues we use high positive charge of TMC. Formation of nano-polyplexes was based on ionic gelation due to TMC and HA electrostatic interactions ability. Both polysaccharides, HA and TMC, were expected to interact through hydrogen bonds and other intermolecular forces. Which can more efficiently entrapped oligonucleotides.



Globular morphology of synthesized NPs has been shown by SEM

Conclusions

A novel chitosan-based nanoparticle with ideal physicochemical properties and desirable loading capacity were formulated for efficient gene therapy.

Keywords

Trimethyl chitosan, Hyaluronic acid, RNAi, Nanoparticle

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Evaluation of anti-bacterial effect of Polymeric Nanofiber Enriched With piperine on staphylococcus epidermidis biofilm

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Introduction

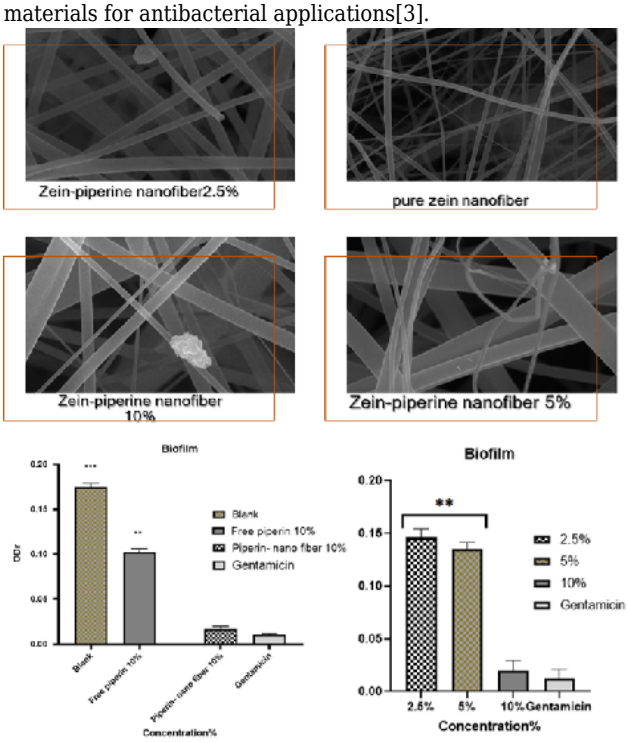
In recent decades, research in the field of nanotechnology has increased significantly. One of the most effective applications in the field of medicine is nanofibers that utilize as carriers for drugs. Electrospinning is one of the most common and cheapest methods of nanofiber production. Zein as a natural protein is currently used in the medical industry as a carrier of drugs. Piperine is a natural alkaloid in black pepper that has many biological properties including antibacterial, anti-inflammatory, and antioxidant effects. The use of suitable piperine solvents and the slow release of piperine from the nanofiber help in overcoming the known limitations of piperine, specifically its low stability and limited bioavailability. This study has been done on synthesized nanofibers containing piperine, produced by the electrospinning technique, for the purpose of antibacterial activity.

Materials and Methods

In this study, piperine was loaded into nanofibers prepared from zein for this purpose, piperine was mixed with zein solution at concentrations of 0, 2.5, 5, 10%, and nanofibers were prepared by electrospinning process. FESEM, XRD, TGA, BET, and FTIR tests were used to evaluate the physicochemical and antibacterial properties.

Results and Discussion

In this study, FESEM, XRD, TGA, BET, and FTIR tests were used to evaluate the physicochemical properties. According to FE SEM images, the morphology of electrospun fibers is uniform and without globules. The X-Ray Diffraction results showed that the Zein was amorphous in the fibers but the piperine was loaded in crystalline form. Also, the results of the BET test revealed that the formulation with a 10% concentration of piperine has a normal pore size. According to the FTIR spectrum, electrospinning had no effect on the secondary structure of Zein, and piperine. Antibacterial tests were conducted against Staphylococcus epidermidis. The nanofibers were 85% antibacterial against Staphylococcus epidermidis. As a result, these nanofibers are very promising materials for antibacterial applications[3].



A) Images of SEM FE electrospun nanofibers loaded. B , C) Adsorption of biofilm at different. (n = 3, Mean ± SD) in the form of sign ** indicates p <0.01 and *** indicates p <0.001 relative to gentamicin.

Conclusions

According to the results of the present study, the fibers obtained from electrospinning can be used as a suitable carrier for piperine as a natural antibacterial agent.

Keywords

Staphylococcus epidermidis; Nanofiber; Electrospinning; Zein; Piperine

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Anticancer effect of colchicine-entrapped niosome on MCF-7 breast cancer cells

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Introduction

Colchicine is driven from Colchicum autumnale and has been used in medicine for a long time. The anticancer effect of colchicine established in recent studies occurs through microtubule depolymerization [1,2]. In this study, we tried to enhance the anticancer effect of colchicine and its bioavailability profile by encapsulating the drug into biocompatible, biodegradable, and efficient cholesterol-based niosomes. Niosomes as drug carriers can delay drug clearance and enhance the entrapped drug's bioavailability and stability [3]. Eventually, we developed our study to investigate the effect of colchicine niosomes on the MCF-7 cells.

Materials and Methods

Colchicine entrapped cholesterol-based niosomes in the presence of span 60 were prepared by the thin-film hydration method. Entrapment efficiency, vesicle size, polydispersity index, and zeta potential were analyzed. Drug release was measured by the dialysis tube. MTT method was used to assess the anticancer effect of pure colchicine and colchicine entrapped niosomes on MCF-7 cells. Moreover, the toxicity of empty niosomes on MCF-7 cells was evaluated too. MCF-7 cells were cultured in the DMEM medium.

Results and Discussion

Niosome's average size was about 324.6 nm. Niosomes showed a zeta potential of -38.5 mV and PDI of 0.755. Drug entrapment efficiency was 97%. In vitro studies revealed a drug release of 63.5% at pH 7.4 during the first 24 hours. The result of the MTT test on the MCF-7 cells showed that the colchicine entrapped niosomes group's viability was considerably lower than the pure Colchicine group. P-value ≤ 0.05 was considered significant.

Conclusions

Entrapped colchicine represents higher growth inhibition of the MCF-7 cell line than pure colchicine. That supports niosomes efficacy in colchicine delivery.

Keywords

Colchicine, Niosome, MCF-7, Breast cancer

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Alpha-Lipoic Acid niosomes: Formulation, physicochemical evaluation and protection effects on cerebral ischemic reperfusion injury in rat model

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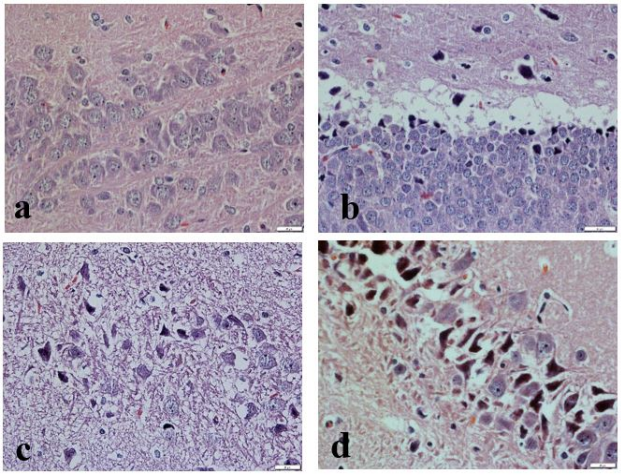
Introduction
Cerebral ischemia reperfusion (I/R) injury is one of the major causes of permanent physical and other irreversible disabilities. Alpha-lipoic acid (ALA) is one of the lipophilic vitamin-like potent antioxidants [1]. Niosomes are considered as carriers that allow the intravenous administration of lipophilic molecules and their crossing through blood brain barrier (BBB), which lead to increased CNS drug uptake [2]. In this study, ALA niosomes were studied based on their morphology, particle size analysis, encapsulation efficiency, physical stability, and in vitro ALA release. The protection of ALA niosomes on Cerebral Ischemic Reperfusion Injury in Rat Model were also investigated.

Materials and Methods
Film hydration method was used to prepare different niosomes composed of Span®, Tween®, and cholesterol at different molar ratio. The release rate was assessed using Franz diffusion cell. Size analysis of lipid vesicles was done by dynamic light scattering method. Rats were subjected to deep anesthesia before inducing cerebral ischemia, then, their internal common carotid arteries were clamped for 15 min and reperfusion was done for 30 min. niosomal formulation was injected intravenously just before declamping.

Results and Discussion
All formulation formed niosomes and stable at 2-8°C for 6 months. Encapsulation efficiency percent of ALA in the selected formulation, was more than 90 % and 60 % of ALA was released after 4h. In the niosomal group, the rate of reduction in complications of cerebral ischemia such as histopathologic changes and acute damage in CNS was higher than other groups. In Wu et al study, the intraperitoneally used ALA and Etanercept for reducing cerebral I/R injury has been studied, and its positive effects on peripheral TNF-α and downregulation of microglial activation have been observed [3].



The rat's hippocampus sections stained with hematoxylin and eosin.

Conclusions
The obtained results show that niosomes can be used as effective drug delivery systems for iv administration ALA in cerebral ischemia.

Keywords
Alpha-Lipoic Acid, niosome, cerebral ischemic reperfusion

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Colchicine entrapped nanoparticle: A strategy to enhance the anticancer effect of colchicine on MCF-7 breast cancer cell line.

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Introduction

Colchicine is an alkaloid that functions as an antimitotic agent by destabilizing microtubules. Because of the severe side effects and complications of colchicine, there is a need for more effective and less toxic formulations [1]. Most natural anticancer drugs are hydrophobic, resulting in low solubility and inadequate concentrations in the target tissue. By connecting the hydrophobic drug with a hydrophilic polymer such as alginate, the combination can cross barriers to cancer cells [2]. Good biocompatibility, biodegradability, accessibility, and low toxicity of alginate make it a desirable carrier.

Materials and Methods

Nanoparticles were prepared by the ionic gelation method using alginate as a carrier. Characterization of the drug release was carried out using the dialysis membrane method. Entrapment Efficiency (EE %), particle size, zeta potential value, and PDI were examined. MCF-7 breast cancer cell line was divided into three groups. Each group was treated with one of the formulated colchicine, free colchicine, or empty nanoparticles, and the viability of cells was assayed by the MTT test.

Results and Discussion

Nanoparticles have an average size of 272.5 nm, polydispersity index (PDI) of 0.69, and zeta potential value of -5.2 mV. The nanoparticle's entrapment efficiency (EE) was 65.51%. Moreover, the release profile of the nanoparticles was studied, and 64.5% of the drug was released within 24 hours. The viability of MCF-7 breast cancer cells treated with colchicine nanoparticles was lower than free colchicine and empty nanoparticles treated cells. The significant amount of P-value was lower than 0.05 in all analytical analyses.

Conclusions

Nanoparticle-treated MCF-7 cells showed the highest growth inhibition. So, alginate nanoparticles can be a suitable carrier for colchicine to enhance colchicine efficacy.

Keywords

Colchicine, Breast cancer, Nanoparticle, MCF-7

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Fabrication of hybrid Scaffolds based on hyaluronic acid/gelatin/chitosan/diatom for bone tissue regeneration

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Introduction

Bone is made up of 60%–70% inorganic material and approximately 30% organic material. Bone tissue engineering is an alternative approach to current therapies available for severe bone defects with poor manifestations of self-regeneration. The 3D polymeric porous scaffolds with higher porosities having homogeneous interconnected pore network are highly useful for tissue engineering, especially for growth of host tissue, bone regrowth. Gelatin and Hyaluronic acid are widely used in biomedicine, due to a good degradability, solubility, biocompatibility. The cationic nature Chitosan is a biodegradable and biocompatible material owing adhesive and antibacterial properties (1). Besides, there have been a number of studies that revealed the biological functions of silica particles supporting bone cell adhesion, bone tissue formation and biomineralization (2). In this study, we created a new composite bone scaffold by gelatin, chitosan, hyaluronic acid and diatom.

Materials and Methods

Chitosan/gelatin/hyaluronic acid/diatom scaffolds were prepared using a freeze-drying method previously described in the literature (3). Scaffolds were characterized by different analyses, e.g. SEM images, X-ray diffraction, FT-IR, mechanical tests, swelling, degradation, porosity and hemolysis test.

Results and Discussion

Open-porous Ge/Cs/Ha/Da scaffolds with varying pore size were successfully synthesized. The porosity, obtained to observe the inert structure of the scaffold the shape and the spatial structure of 3D freezing-dry method (fig a). FT-IR was used to identify the molecular composition and demonstrated the crosslinking of Ge/Cs/Ha/Da hybrids using EDC/NHS crosslinking agent (fig b) (3). XRD patterns were recorded to determine the structural phases in composite scaffolds. The results revealed diatom is consistent with the crystalline silica (fig c). The compressive modulus was determined for scaffolds and is highest for scaffold with diatom 10% (fig d). Liquid uptake and porosity both of them decreased with the increasing amount of diatom added to the sample, related with the samples swelling behavior and porosity (Fig e,f).The biodegradation of a biomaterial depends largely on its composition and structure (fig g). Hemolysis test shown all scaffolds have hemocompatibility (fig h).

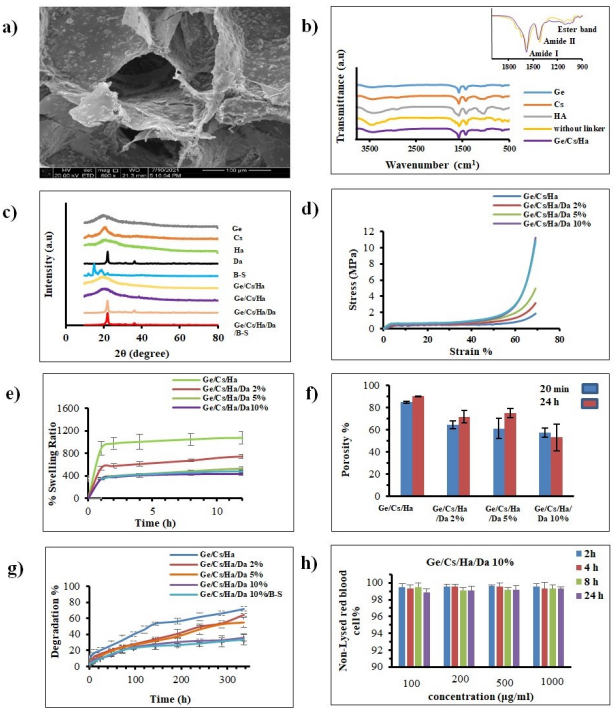

Figure a-h) characterization of schaffolds Ge/Cs/Ha/Da/B-S

Conclusions

We have shown here that the scaffolds composed of Ge/Cs/Ha/Da/B-S exhibited suitable mechanical properties close to bone tissue engineering. It was fabricated by freezing and lyophilizing methods. The porosity and high surface area of scaffolds affected the higher water uptake. Web-like diatom on the matrix played an important role in the surface charge, which can affect the mechanical properties. The swelling of gelatin allowed the expansion of scaffold's matrix in the stimulated body fluid, which makes enough space for the cells to attach and infiltrate into the scaffolds.

Keywords

gelatin, chitosan, hyaluronic acid, diatom, scaffold

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Bioinspired Highly Strong, Porous and Photoactive Cellulosic Scaffold for Bone Regeneration

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Introduction

Bone-related diseases, such as cancers, infection, and trauma, are common clinical problems that result in hardly recoverable bone defects, which cause a burden to healthcare systems due to the prolonged hospitalization and long healing process. NIR-responsive scaffolds coated with photothermal agents can absorb near-infrared (NIR) light and convert it to thermal energy. The generated heat can be controlled to maintain the temperature of the defect site to 39-40 °C as it is approved to assist in enhancing the proliferation of human mesenchymal stem cells and promoting osteogenesis. In this study, mild heat-induced osteogenesis is studied by a biodegradable cellulose-based scaffold coated with Bismuth Sulfide nanoparticles (NPs) while its pores are filled with gelatin-hyaluronic acid thermo-responsive hydrogel.

Materials and Methods

Bismuth Sulfide NPs were prepared using a simple chemical reaction and plant-derived cellulose scaffolds (C-scaffold) were coated with NPs entirely to generate Bi-scaffold. Then the scaffolds were immersed in gelatin-HA hydrogel for 4 hours (Bi-Gel scaffold). Following that, the scaffolds were dried by freeze-drying. Scanning electron microscope (SEM) was used to characterize the morphology and structure of the scaffolds. Elemental analysis, porosity, thermo-gravimetric analysis (TGA) and antibacterial activity of the NPs and scaffolds were evaluated. In addition, the mechanical properties of scaffolds, in vitro photothermal activity, and in vivo toxicity of Bismuth Sulfide NPs and scaffolds were assessed.

Results and Discussion

Transmission electron microscopy (TEM) image shows that Bismuth Sulfide NPs have a uniform spherical shape with an average diameter of about 5 nm. The FE-SEM images of scaffolds demonstrated that the scaffold coated with NPs and impregnated with gel while indicating desirable porosity. The elemental analysis of Bi-scaffold confirms that the scaffold coated with Bismuth Sulfide sufficiently. The compressive strength of Bi-Gel scaffold is approximately about 17.2 MPa, which is much higher than trabecular bones (Mean value= 3.9 MPa). The photothermal performance of the Bi-scaffold showed that the temperature increased rapidly to 76°C after NIR laser irradiation at 1.5 W/cm2, which confirm the high photothermal conversion efficiency of the scaffold. The scaffolds showed very potent antibacterial effect against E. coli and S. aureus under NIR irradiation.

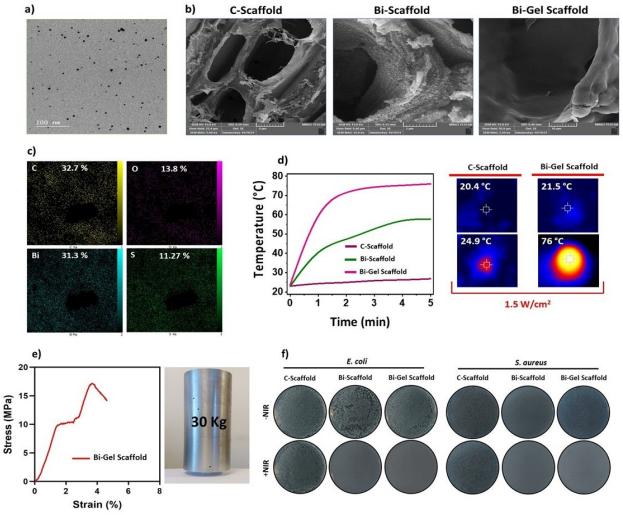

Figure 1. a) TEM image of the NPs, b) FE-SEM images of different scaffolds, c) EDAX of Bi-scaffold, d) Photothermal activity of different scaffolds, e) Mechanical properties of Bi-Gel scaffold, f) Antibacterial activity of different scaffolds.

Conclusions

The Bismuth Sulfide coated cellulosic scaffold has great potential in orthopedic applications due to good NIR-mediated and hydrogel-assisted osteogenic performances and this study provides new insights into the design and fabrication of new-style osteoimplants for bone regeneration.

Keywords

Cellulose Scaffold, Hydrogel, Photothermal Therapy, Bone regeneration

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Development of antibacterial and highly protective facemask for prevention of COVID-19 infection

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Introduction

The recent onset of coronavirus disease 2019 (COVID-19) has resulted in a global pandemic and major health crisis. Therefore, the use of facemasks and other face-covering textiles has become ubiquitous all around the world. However, because of the extensive use by the community, the demand for facemasks has exceeded supplies leading to a global shortage. On the other hand, the available evidence indicated that the many commercial and handmade respiratory protection masks that are currently used by the public show undesirable and insufficient protection due to the nanoscale size of the virus. This is highly challenging in protecting clinicians and other health care workers from severe acute respiratory syndrome coronavirus infection. Therefore, in the present study, we aimed to develop an antibacterial and antiviral facemask with desired protection and pressure drop.

Materials and Methods

Silver nitrate (AgNO3), polyvinyl alcohol (PVA), PA6, ethylene glycol, formic acid (65%), acetic acid (98%), ammonia solution (28-30%), and ethanol were purchased from Sigma Aldrich (Germany), and span bond was supplied from the market.

Results and Discussion

From the respective TGA diagram of the coated sample, the weight percent of deposited silvers was measured as 8.5%. The SEM image of resultant fabrics also showed a uniform coating of silver on span bond strands. The SEM image of electrospun nanofibers also revealed a homogenous, bead-free, and random-oriented morphology. The random-oriented morphology of the resultant nanofibers increases the tortuosity of the matrix and could result in the enhanced particle removal ability of the substrates. Measurement of the particle size and particle size distribution of coated samples revealed that the particle size of deposited silver on fabrics is on the scale of nanometer and with increasing the sonication time larger particles were formed. The XRD pattern of the samples showed characteristic diffraction peaks of silver at 2θ value of 38.1°, 44.45°, 64.55°, 77.40° corresponding to the (111), (200), (220) and (311) planes of metallic silver, respectively. The mechanical properties of coated and

Conclusions

Considering the aim of the present study, the results revealed that the silver nanoparticles were successfully deposited on the fabric surface. Electrospinning of PA6 and PVA on the coated fabrics was also conducted for increasing the tortuosity of matrixes and enhancing the filtration efficiency of fabrics. Altogether, the silver-coated and fiber-reinforced substrates exhibited a desired antibacterial activity, cell viability, and filtration efficiency. Therefore, these two techniques, namely sonochemically coating method and electrospinning method could be applied for preparing products with enhanced properties in different fields of science and technology such as the development facemask for protection against SARS-CoV-2 coronavirus and other possible applications such as air filtration, food packaging, textile industries, etc.

Keywords
Covid-19, Sonochemistry, electrospinning, facemask.

References

Preparation and evaluation of chitosan gel containing Ficus carica extract

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Introduction

Wound is a substantive menace across the board both in terms of public health and economic. Medicinal plants have been used since ancient times as remedies for simple wound healing. Their therapeutic use is not only still popular today as past but also due to advancements that have been made in phytochemical and analytical methods, plants are becoming more attention grabbing in providing effective treatments for wound healing .Ficus carica (Moracea) .F. carica is one of the medicinal plants used traditionally for treatment of inflammatory diseases .In addition , chitosan is a functional material for wound treatment due to its hemostatic effect, ability to inhibit microbial growth and accelerate wound healing. The present study aims to investigate the wound healing activity of ethanolic extract of leaves of F. Carica in the form of chitosan-based gel.

Materials and Methods

Ethanolic extracts of leaves of the F. carica were prepared using maceration method and then different gel formulations containing 12.5, 25 and 30 percent of extract were prepared.. Finally, formulations were assessed for gel physicochemical properties like homogeneity, Spreadability, PH, viscosity(using viscometer), mechanical properties and stability.

Results and Discussion

According to physicochemical studies, three formulations of those which had following characteristics selected; homogenous and no undissolved particles , good spreadability on the hand , moderate viscosity , forming flexible film on the hand , lack of aggregates, gentle movement on the glass and the pH between 5-6 within the range of skin pH.

Conclusions

Our results demonstrated that chitosan-based gels containing F.carica can be prepared with desired physicochemical properties as a candidate for wound healing. It is noticeable that animal studies are ongoing in our laboratory.

Keywords

Ficus carica , chitosan ,wound ,physicochemical properties

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Development, statistical optimization and in vitro/ in vivo characterization of an intelligent hydrogel containing methylated N-(4-N, N-dimethylaminobenzyl) chitosan for glucose-responsive insulin delivery

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Introduction

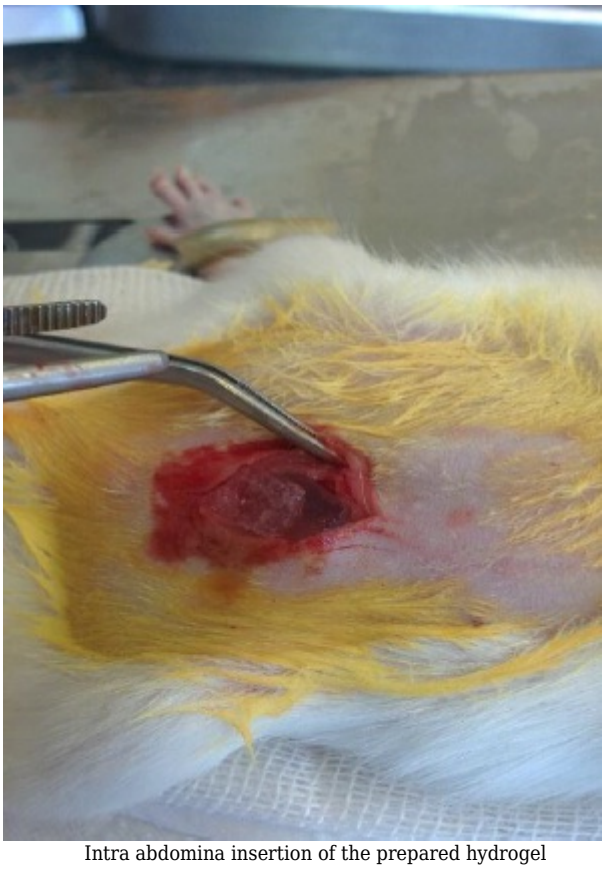
The aim of this study was to develop an intelligent, glucose-responsive hydrogel composed of methylated N-(4-N,N-dimethylaminobenzyl) chitosan as a quaternized and aromatized derivative of chitosan.

Materials and Methods

In this study, a cross-linked hydrogel, incorporating boric acid (BA), was prepared from the synthesized chitosan derivative. The preparation of hydrogel was statistically optimized using box-behnken response surface methodology. The chemical structure and morphology of the optimized hydrogel were examined using FT-IR spectroscopy and scanning electron microscopy, respectively. Furthermore, the glucose-responsive behavior of the prepared hdyrogel was evaluated by in vitro release studies. Finally, the efficacy of the prepared hydrogel in glucose-responsive insulin delivery was studied in vivo by implementation of the hydrogels in male wistar rats and their blood glucose levels were evaluated in the pre-determined time intervals.

Results and Discussion

The optimized hydrogel with proper characteristics was prepared. Following 480 min of incubation, the in vitro release study demonstrated 26.1±1.84%, 52.7±3.11% and 78.9±3.85% of cumulative insulin release in glucose-free-, glucose 3%- and glucose 5%- phosphate buffer, respectively. Finally, the obtained in vivo results demonstrated 1.5-fold reduction in blood glucose level in diabetic animals in comparison with non-diabetic ones.



Intra abdomina insertion of the prepared hydrogel

Conclusions

The obtained data suggests that the hydrogel can efficiently pose glucose-responsive properties for insulin delivery.

Keywords

Insulin, Glucose-Responsive; Hydrogel, methylated N-(4-N, N-dimethylaminobenzyl) chitosan, Boric acid, Poly Vinyl Alcohol (PVA)

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Preparation and In vitro / In vivo evaluation of an intelligent drug delivery system composed of a hydrogel prepared from 4-N,N-dimethyl aminobenzyl chitosan for glucose-responsive delivery of repaglinide

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Introduction

Now a days, diabetes is the most common metabolic diseases and the prevalence is increasing in our societies. Traditional methods of using glucose-lowering agents do not precisely control the blood glucose level. Therefore, for prevention of both hypoglycemia and hyperglycemia in diabetic patients, development of a glucose-responsive drug delivery system for intelligent delivery of glucose- lowering compounds is highly interesting. The purpose of the present study was to preparation and in vitro / in vivo evaluation of a glucose-responsive drug delivery system composed of the glucose-responsive hydrogel prepared from quaternized aromatic derivative of chitosan for intelligent drug delivery of repaglinide.

Materials and Methods

Firstly, a quaternized derivative of chitosan (4-N,N-dimtehyl aminobenzyl chitosan) was synthesized and the structure was ascertained using 1H- NMR. Thenafter, the optimized hydrogel was prepared using central composite response surface methodology. The independent variables were the concentrations of chitosan, boric acid and poly vinyl alcohol while the dependent variables were the swelling ration in 0% glucose, the swelling ratio in 5 % glucose, the loading efficiency of repaglinide in the hyrogel structure, the cumulative percent of release in 0% glucose and the cumulative percent of release in 5% glucose. The hydrogel was prepared using three cycles of freeze-thaw. The prepared hydrogel was characterized by FT-IR and SEM microscopy. Finally, the efficacy of the prepared hydrogels was evaluated in vivo by intradermal administration of hyrogels in both diabetic and non-diabatic rats.

Results and Discussion

1H-NMR studies confirmed the synthesis of 4-N,N-dimethyl amini benzyl chitosan . The optimized hydrogels were characterized and the data demonstrated 96.1±3.58% of drug loading. The hyrogel demonstrated 321.68±1.72% and 678.28±1.81% of swelling in glucose 0% and glucose 5% , respectively. Moreover, the cumulative drug release were 26.36±2.62% and 67.31±1.88 in glucose 0% and glucose 5%, respectively. The SEM studies demonstrated formation of desirable porous hydrogel. As the in vivo study, the plasma concentration of repaglinide in diabetic and non-diabetic rats were reported as 8.70±1.22 µg/ml and 1.93± 0.87 µg/ml, respectively.

SEM images of the prepared hydrogel

Conclusions

It was showed that the prepared hyrogel can release the repaglinide as a glucose-lowering agent in response to glucose level of plasma.

Keywords

4-N,N- dimethyl aminobenzyl chitosan, boric acid, Glucose-responsive hydrogel, repaglinide, central composite response surface methodology

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Effects of formulation composition on the characteristics of orodispersible films prepared by semisolid extrusion 3D printing

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Introduction

Response surface methodology (RSM) is a collection of statistical and mathematical techniques used for developing, improving and optimizing processes in which the response of interest is influenced by several variables. Using this technique, we can establish relationship between the response and the independent variables [1]. The aim of this study was to investigate the effects of formulation composition on the physicochemical and drug release properties of orodispersible films prepared by semisolid extrusion 3D printing, using a response surface methodology.

Materials and Methods

Beeswax/paraffin and Poly vinyl alcohol (PVA) as water insoluble and water soluble polymers, respectively, hydroxypropylmethylcellulose (HPMC) (drug release retardant) and borax (emulsifying agent) were the four independent factors and drug release, swelling index, disintegration time and flexural strength as responses utilized for the study. The responses were fitted to a full quadratic model and P-values for each of the factors were used to determine their significance on the film characteristics.

Results and Discussion

Results demonstrated no drug excipient interaction and excellent content uniformity. The Sem images show a layer-by-layer printing well, Fig. 1. The drug release was found to be significantly affected by all the four factors and no interaction between factors was observed. A significant interaction was observed between PVA and beeswax/paraffin for disintegration time of films. For swelling index, a significant interaction was found between PVA and HPMC. The in vitro % drug release was directly correlated with HPMC and PVA content and varied from 53–79% at 4 h [2].

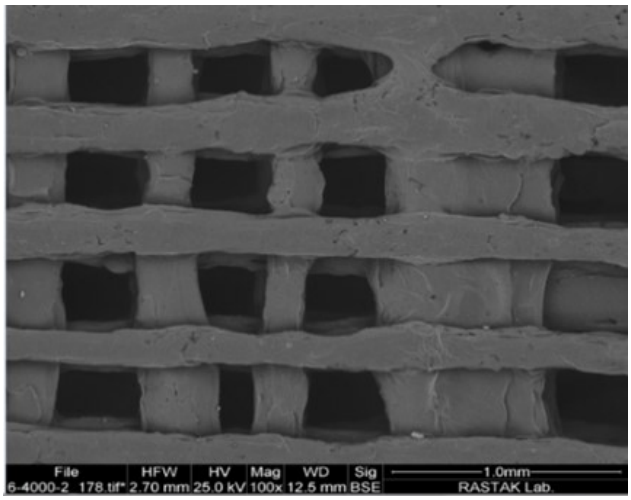

Fig1.SEM of patch

Conclusions

The influence of formulation parameters on Oral betamethasone films were elucidated, indicating the use of semisolid extrusion 3D printing as a feasible method for film preparation.

Keywords

experimental design, 3D printing, orodispersible films, optimization, swelling index

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Formulation and Evaluation of stealth liposomal fluoxetine on memory and cognition performance

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Introduction

Stealth liposomes form an important subset of liposomes, demonstrating prolonged circulation half-life and improved safety in vivo. Selective serotonin reuptake inhibitors (SSRIs) have been reported to increase cognitive performance in some clinical studies of Alzheimer's disease (AD) [1]. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) which enhances cognitive performance and has a large volume of distribution. The use of nanocarriers such as liposomes may enhance drug transport through the Blood-Brain-Barrier (BBB) in neurodegenerative disease and target relevant regions in the brain. Here we formulated and characterized physicochemical properties and the effects of stealth liposomal fluoxetine on cognitive behavioral paradigms [2].

Materials and Methods

Stealth liposomes were prepared by ionic gelation method with Sodium tripolyphosphate / Chitosan / Polyethylene glycol ratio of 1: 5: 20 The liposomes were characterized by Dynamic Scattering Light (DLS), Zeta Potential (ZP), Fourier Transform Infrared (FTIR), Scanning Electron Microscopy (SEM). Fluoxetine release testing was performed at a PBS media. The effects of liposomal fluoxetine on memory, cognition and IGF-1 protein expression are investigating.

Results and Discussion

The average size of liposomes was observed to be 240.2 nm with PI 0.243. Encapsulation efficiency was measured by reverse-phase HPLC at about 53%. The release pattern of the drug is slow release and the liposomes released 75% of the fluoxetine within 4 hours, according to Fig1. Animal tests are also underway.

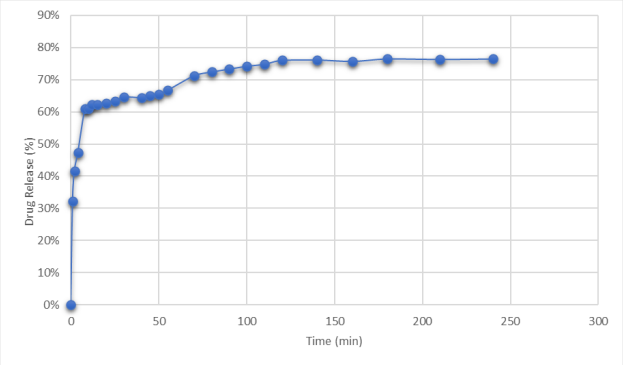

Fig1. Pattern of drug release

Conclusions

Chitosan and Chitosan/Polyethylene glycol liposomes were successfully prepared to encapsulate Fluoxetine but the encapsulation efficiency in Chitosan/PEG liposomes were lower than chitosan liposomes. They did not differ much in size and zeta potential. The aggregation between Chitosan/Polyethylene glycol liposomes reduced and drug release improved. Preliminary animal studies have clearly demonstrated the potential of stealth liposome in extending the circulation half-life of fluoxetine and in reducing systemic toxicity. More studies can be carried out to further investigate the in vivo PK and PD characteristics.

Keywords

Fluoxetine, Blood-Brain-Barrier, stealth liposomes, Chitosan

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Nanocrystalization of Pioglitazone by Precipitation Method

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Introduction

Introduction: Poor solubility in an aqueous medium limits the use of many drugs. Different methods have been adopted to promote the rate of dissolution of slightly water-soluble drugs. Crystallization improves solubility, and bioavailability by increasing the surface area of slightly water-soluble drugs. Pioglitazone (PGZ), which is a class II Biopharmaceutical Classification System drug has a slight solubility in water and a slow rate of dissolution, which may have a negative effect on its metabolism leading to a therapeutic failure. The aim of this study was to improve the solubility of PGZ-HCl; an antidiabetic drug-using precipitation method.

Materials and Methods

Materials and methods: Formulations were prepared with polyethylene glycol 6000 and isomalt using different speed of homogenizer and quantity of solvent by precipitation method. Drug-polymer interactions were examined using differential scanning calorimetry (DSC), and Powder X-Ray Diffraction (PXRD). Surface structure were shown by SEM photographs.

Results and Discussion

Results: The particle size was significantly decreased and solubility was enhanced with increasing speed, ethanol solvent and increased stabilizer, however very high amount of stabilizer resulted in a decrease in solubility.

Conclusions

Conclusion: This result however showed that the solid dispersion technique is a potential method for increasing the dissolution profile of a poorly aqueous soluble agent.

Keywords

pioglitazone, nanocrystal, precipitation method, PEG 6000, isomalt

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Development of Finasteride loaded and Minoxidil loaded Chitosan nanoparticles as Potential carriers for local drug delivery in alopecia

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Introduction

Androgenic alopecia (AGA) is a condition with a high prevalence worldwide that affects males and females. Finasteride (FNS) has been approved and used orally to treat AGA; however, systemic effects on other androgen-dependent tissues cause serious side-effects. Oral FNS will reduce DHT levels by inhibiting 5alpha reductase enzyme which can lead to some systemic side effects. On the other hand, topical administration of FNS can be a proper drug delivery strategy in order to avoid the systemic adverse reactions. Also, Minoxidil (MX) is a drug which is broadly used as a therapy for AGA, MX mediates its action by anagen phase prolongation in the hair follicles. But it has variable success rate in the treatment of AGA. However, topical dosage forms of FNS and MX is not efficient and using nanoparticulate systems could be a good alternative route for this issue. This study targets the preparation of FNS and MX chitosan nanoparticles (NP) and evaluates their physicochemical charactristics.

Materials and Methods

Chitosan nanoparticles loaded with FNS and MX prepared by ionic gelation method and their size, zeta potential and loading efficiency were evaluated. The optimum formulation achieved by changing CHI/TPP ratio, based on their highest percentage of loading efficiency and best particular properties.

Results and Discussion

The most appropriate FIN/CHI and MX/CHI nanoparticle formulations contain 15:1 and 11:1 CHI/TPP ratios respectively. Loading efficiency of FNS into chitosan nanoparticles was 99.8% and for MX chitosan nanoparticles was 93%. Results of DLS showed that the size of FNS/CHI NP is about 105 nm and their zeta potential about 35.2 mV. Also, the size of MX/CHI NP is about 101 nm with a zeta potential of +17 mV.

Conclusions

Accordance to the results, FNS/CHI NP and MX/CHI NP can be a good candidates as local delivery systems of FNS and MX for treating of alopecia.

Keywords

nanoparticle, chitosan, finasteride, minoxidil, alopecia

References

Synthesis, Characterization, and in vitro evaluation of a bio star-hyperbranched polyurethane film based on D-glucose-poly (3- hydroxybutyrate-co-3-hydroxyvalerate) for sustained release of insulin

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Introduction

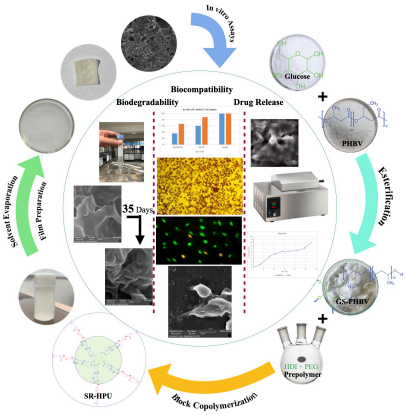
Daily insulin injection is one of the most common ways to treat diabetes mellitus (DM). Due to the short half-life of insulin, repeated injections of this drug are required, which causes the patient suffering and poor patient adherence. As a result, a novel 3D porous polyurethane network (SR-HPU) was designed and synthesized, consisting of a star-shaped hydrophobic glucose-based PHBV (GS-PHBV) core, with the goal of application as a sustained release delivery system for insulin.

Materials and Methods

For this purpose, a star-shaped PHBV based on the glucose core was synthesized by direct esterification of the carboxylic end-groups of the PHBV with hydroxyl groups of glucose as the multifunctional initiator in the presence of methane sulfonic acid (MSA) as the catalyst. To synthesize SR-HPU, hexamethylene diisocyanate (HDI) through the prepolymerization stage was added to the polyethylene glycol (PEG) in the presence of the DABCO® T-9 catalyst. Subsequently, the GS-PHBV solution was added to the prepolymer solution to afford the star-block copolymer through block copolymerization. The insulin-loaded film (INS-PUF) was obtained by a solvent evaporation method.

Results and Discussion

1HNMR and ATR-IR results confirmed the successful synthesis of SR-HPU and INS-PUF. TGA, XRD, and WCA analysis demonstrated that due to the block copolymerization of GS-PHBV with HDI and PEG, the crystalline pattern of the final film was disrupted, which led to an increase in hydrophilicity. The in vitro degradability of SR-HPU was investigated by evaluating the morphological changes, and gravimetric measurements after soaking the copolymer in PBS (pH 7.4 at 37°) for 35 days. XRD and EDX mapping results revealed that insulin is uniformly present within the SR-PU matrix. In vitro cytocompatibility studies performed over 24 h indicated that SR-PU was nontoxic to mouse fibroblast cells (L929). In vitro release studies from INS-PUF showed that a prolonged drug release pattern has been achieved for 56 days.



Graphical Abstract

Conclusions

Based on these results, 3D networks SR-HPU due to supramolecular structure and the presence of PU and PEG blocks exhibited unique properties and improved the natural defect of PHBV. Therefore, the biocompatible and biodegradable SR-HPU elastomer synthesized with great drug release behavior can be considered as potential candidates for sustained release drug delivery systems.

Keywords

Star-hyperbranched Polyurethanes, PHBV, Drug Delivery, Insulin, Biomaterials

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Injectable Photothermally Active Hydrogel Incorporated with CuO Nanosheets for Simultaneous Skin-Tumor Therapy, and Multidrug-Resistant Infection-Induced Wound Healing

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Introduction

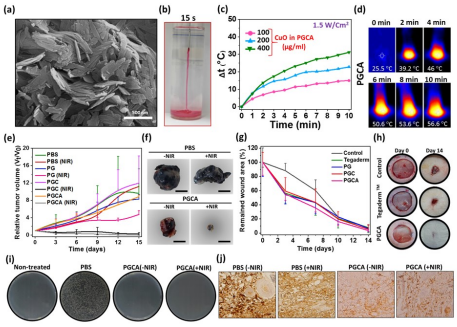
Melanoma is the most aggressive skin cancer, resulting in significant mortality. The conventional treatment process includes surgical excision followed by chemotherapy and radiotherapy (1). However, the multidrug-resistant bacteria infected-wound and severe side effects of chemotherapy and radiotherapy are still important challenges. So, there is a high demand for the development of novel multifunctional biomaterials that can simultaneously treat cancer and infected wounds for efficient skin regeneration. In recent years, photothermal therapy has made significant breakthroughs as a promising strategy to ablate cancers and bacteria by hyperthermia (2). Copper oxide (CuO) is an attractive photoactive agent, which can show combined antimicrobial and photothermal effects for regenerative applications (3). Incorporating these nanoparticles along with regenerative drug molecules inside injectable hydrogels would allow the design of advanced formulation for melanoma therapy and tissue repair.

Materials and Methods

CuO nanosheets were synthesized by the precipitation method. Subsequently, PG hydrogel was prepared through the chemical crosslinking between poly (methyl vinyl ether maleic acid)-gelatin, followed by the incorporation of CuO and allantoin to form PGCA hydrogel. Physicochemical characterization, injectable property, and photothermal performance of the hydrogel were assessed. Furthermore, antibacterial activity, in vivo toxicity, wound healing assessment, and photothermal anti-cancer therapy of the hydrogel were evaluated.

Results and Discussion

CuO nanosheets with lengths ranging from 100 to 400 nm were successfully synthesized (Fig. 1a). The injectability of hydrogel was visualized through a 21-gauge needle without any clogging (Fig. 1b). CuO nanosheets revealed good photothermal efficiency which could ablate cancer cells within 10 min at 1.5 W/cm^2 power density at the concentration of 400 µg/ml (Fig. 1c-f). Moreover, by exploiting the intrinsic properties of CuO and Allantoin, the hydrogel supported proliferation and angiogenesis of cells and resulted in wound healing acceleration after cancer ablation (Fig. 1g, h). In addition, the abscess model results demonstrated that CuO could effectively kill bacteria owing to the synergistic effect of hyperthermia and inherent antibacterial properties (Fig. 1i, j). Finally, the histopathological evaluation of the main organs of rats showed no organ damage, like necrosis and inflammation.



(a) Electron microscopy image of CuO. (b) Injectability test of hydrogel. (c,d) Thermal plots and Infrared thermal photographs of PGCA. (e,f) The in vivo tumor suppression assessment. (g,h) The wound healing evaluation. (i,j) The abscess model.

Conclusions

In this study, an injectable multifunctional hydrogel containing CuO and allantoin was prepared to simultaneously ablate melanoma cells and bacteria. Moreover, the hydrogel effectively promoted wound healing via stimulating fibroblast proliferation and enhancing angiogenesis.

Keywords

Injectable hydrogel, Copper oxide nanosheet, Photothermal therapy, Anti-infection, Melanoma, Wound healing, Combined therapy.

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Preparation and entry assessment of hydrophobic dye-loaded chitosan nanoparticles into LNCaP cell line

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Introduction

Prostate cancer is high-prevalence cancer in men. Enzalutamide, with poor water solubility (logP=3.75), is used in advanced prostate cancer. Chitosan nanoparticles are widely used for drug delivery. In this study, a hydrophobic dye-coumarin-6 (logP=4.9) was loaded into the chitosan nanoparticles. Then, encapsulation efficiency (EE) and cellular uptake of nanoparticles were evaluated.

Materials and Methods

Chitosan nanoparticles were prepared by the ionic gelation method [1]. Aqueous suspension of coumarin-6 was poured into the chitosan solution, and then different concentrations of sodium tripolyphosphate (TPP) solution were added to the dispersion, resulted in nanoparticle formation. Next, prepared nanoparticles were kept at 4°C for 5 days to precipitate the unloaded dye. After that, the supernatant was collected and freeze-dried. The EE of the dye in the nanoparticles was measured by HPLC. For entry assessment, a cultured LNCaP cell line was treated with the prepared dispersed nanoparticles in water and free coumarin-6 solution for 2 hours. Finally, cellular uptake of dye-loaded nanoparticles was assessed by fluorescent microscope and HPLC [2].

Results and Discussion

The size of the prepared nanoparticles was around 200 nm. The nanoparticles' EE was about 3%. Microscopic results proved cellular uptake of free coumarin-6 and coumarin-6-loaded nanoparticles into cells. Furthermore, HPLC results showed that about 17% and 23% of used coumarin-6 was entered into the cells in nanoparticle- and free coumarin-6-treated cells, respectively. The results were in line with Trapani and colleagues' study [1].

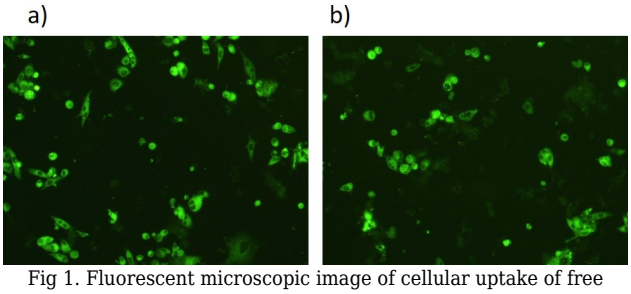

Fig 1. Fluorescent microscopic image of cellular uptake of free coumarin-6 (a) and coumarin-6-loaded nanoparticle (b) after 2 hours treated into LNCaP cell line

Conclusions

Studies displayed that chitosan nanoparticles are suitable vehicles for hydrophilic drugs, our results exhibited that these kinds of nanoparticles have the potential to be used for the delivery of potent hydrophobic drugs.

Keywords

chitosan nanoparticles, Coumarin-6, HPLC, LNCaP, Cellular uptake

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A simple approach for assessment of IC50 of bipyridine compounds without using complex descriptors: New Anti-cancer designing

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Introduction

The anticancer compounds should be potent enough to reduce or kill cells, and this attribute is measured with the IC50 parameter, which is the suitable amount of anticancer drugs can inhibit the multiplication rate of tumor cells by 50 percent [1]. This study investigates the Quantitative structure-activity relationship (QSAR) of 16 anticancer compounds based on bipyridine on Hela cells with Multiple Linear Regression (MLR).

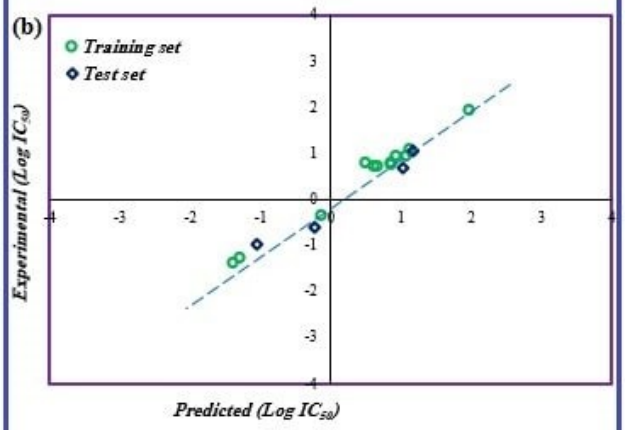
Materials and Methods

Anti-cancer structures based on bipyridine with their IC50 (Figure 1a) parameters against Hela cells were collected from different experimental work (https://uupload.ir/view/ic503_d5ym.docx/). All the compounds were optimized and computed with the Hyperchem and Dragon softwares to obtain the MLR model by SPSS software [2,3]

Results and Discussion

Among the 16 anticancer crystal compounds, 12 were selected randomly as the training set, and 4 were chosen as the test set. This work studied calculated descriptors and IC50 relationship to extracted best descriptors for modeling which followed as R7u+ (R maximal autocorrelation of lag 7/unweighted GETAWAY descriptors), E3u (3rd component accessibility directional WHIM index/unweighted), and BELv2 (the lowest eigenvalue n. 2 of Burden matrix/weighted by atomic van der Waals volumes). The BELv2 descriptor has a great result on IC50 because of the negative effect. R2 and MSE were 0.981 and 0.017 for the training test, the mentioned parameters were 0.970, and MSE 0.062 for the test set, respectively Figures 1b,c. Log IC50 = 20.225-85.939×R7u+–9.432×BELv2+2.053×E3u

(a)	IC_{50}	Exp. Log IC_{50}	Pred. Log IC_{50}	Dev.	CCDC No.
Training set					
1.	0.050	-1.301	-1.257	-0.044	[952858]
2.	0.040	-1.398	-1.363	-0.035	[952860]
3.	4.530	0.656	0.717	-0.061	[1916696]
4.	7.210	0.858	0.752	0.106	[1916697]
5.	3.060	0.486	0.802	-0.316	[1917997]
6.	8.470	0.928	0.939	-0.011	[1918001]
7.	4.110	0.614	0.731	-0.117	[1918004]
8.	11.880	1.075	0.921	0.154	[1918010]
9.	92.160	1.965	1.947	0.017	[2013057]
10.	0.730	-0.137	-0.331	0.194	[1048414]
11.	13.410	1.127	1.088	0.040	[1571873]
12.	7.060	0.849	0.776	0.073	[1842068]
Test set					
13.	0.580	-0.237	-0.583	0.346	[952857]
14.	0.090	-1.046	-0.971	-0.074	[952859]
15.	10.620	1.026	0.701	0.325	[1918007]
16.	15.100	1.179	1.043	0.136	[766526]



(C)	Model	Sets	R^2	MSE	Q^2
	$LogIC_{50}$=20.225–85.939× R7u$^+$–9.432× BELv2–2.053×E3u	Training set.	0.981	0.017	0.982
		Test set.	0.970	0.062	1.000

Figure 1. a: Training and test sets , b: Experimental versus predicted values diagram, c: Statistical parameters.

Conclusions

According to QSAR results, a novel, simple MLR model can be used for other similar compounds. This work was satisfying and robust for developing a future view of the anticancer carrier and suitable compounds.

Keywords

QSAR, MLR, IC50, Bipyridine

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Computational study of Chitosan-conjugated acrylamide-Au nanocomposite: New nanocarrier designing for drug delivery

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Introduction

Drug delivery systems (DDSs) are applied to treat various types of diseases more efficiently and selectively. The utilizing different nanoparticles in DDSs is of special importance nowadays. Among the nanoparticles, polymers and metals can be actually practical as nanocarriers. Chitosan (Cs) and Gold nanoparticles (AuNPs) have been used in drug delivery due to their non-toxicity, biocompatibility, and stability features [1]. In this study, chitosan conjugated acrylamide in the presence of gold nanoparticles (CsAAu), was studied as a practical nano vehicle to adsorb 5 fluorouracil (5-Fu) and cyclophosphamide (CYP) as anti-cancer drugs in Material studio 2017.

Materials and Methods

The chitosan conjugated acrylamide and (AuNPs) and drugs were optimized for the drug delivery system based on DFT calculations in Material Studio 2017. The adsorption locator module was used for the adsorption of the drugs in the presence of 10 water molecules [2].

Results and Discussion

The optimization of structures for chitosan conjugated acrylamide and anticancer drugs are shown in Figures 1(a - d). The optimized energies for drugs were obtained at -513.85 and -1789.40 Ha for 5-Fu and CYP respectively. The adsorption of 5-Fu and CYP in the presence of 10 water molecules was obtained at -75.50 and -2216.90 Kcal/mol, respectively. According to the results, CYP was greatly better than 5-Fu due to its lower energy [3]. Hydrogen bonds are really important in the adsorption of the drugs during the loading process (Figures 1(e and f).

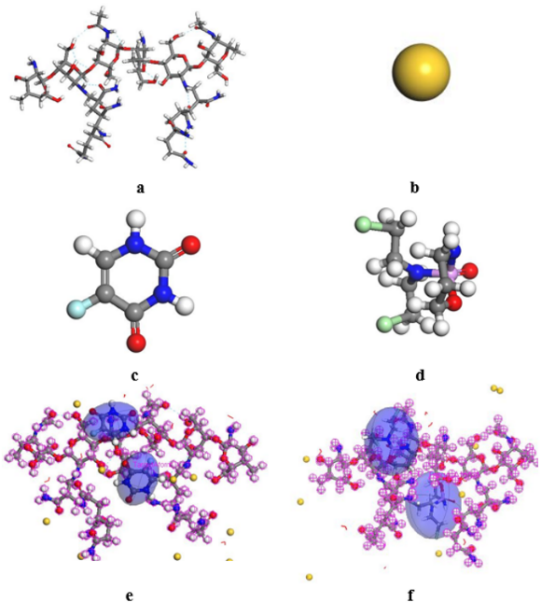

Figure 1. a: Optimized chitosan conjugated acrylamide , b: optimized Au, c: optimized 5-Fu, d: optimized CYP, e: adsorption of 5-Fu, f: adsorption of CYP

Conclusions

Based on the quantum studies, the adsorption of 5-Fu and CYP on CsAAu has been calculated in Material studio 2017 software. The adsorption of CYP was high compared with 5-Fu due to its low energy.

Keywords

Adsorption, Quantum chemical calculations, Drug delivery, Chitosan, Monte Carlo Computer Simulation

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Monte Carlo computer aided simulation of advanced CNT-conjugated Folic acid as a pharmaceutical carrier: Novel drug delivery system

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Introduction

The drug delivery systems (DDS) are novel recommended therapies against severe lethal diseases, e. g. cancer. The carbon nanotubes (CNTs) are one of the most useful substrates for DDS, used in vitro and in vivo tests. In targeted drug delivery, Folic acid (FA) can match drugs to targeted areas [1]. In this work, the computational methodology was used to recognize the loading of anticancer drugs based on the density functional method (DFT) in Material Studio 2017. The adsorption of two drugs carboplatin (CP) and Imatinib (IMB) was computed on the nanocarrier CNT.

Materials and Methods

The carbon nanotube linked with ethylenediamine-linked folic acid (CNEF) and anticancer drugs optimized by the DMol3 module in Materials Studio 2017 based on the DFT method. Then, adsorption of the anticancer drugs was performed by the adsorption locator module in the presence of 10 water molecules [2].

Results and Discussion

Following the design of all structures, optimization of the nanocarrier and drugs was implemented with the aforementioned method. The optimized models for CNEF and drugs are demonstrated in Figures 1(a-c). The optimized energies for CP and IMB have obtained -17968.36 and -1581.38 Ha, respectively. The adsorption of CP and IMB on the CNEF was obtained at -274.23 and -147.81 Kcal/mol. According to the results, the adsorption of CP was more potential than CP due to its lower energy Figures 1(d and e) [3].

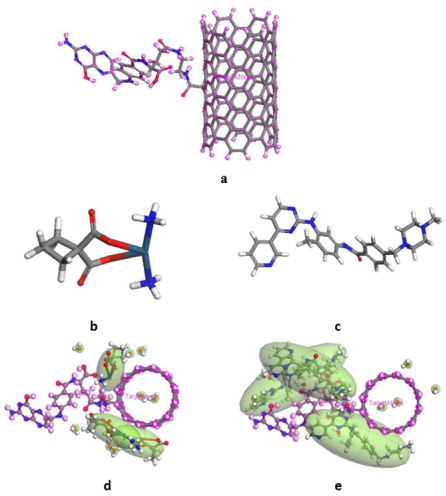

Figure 1. a: Optimized CNT, b: optimized CP, c: optimized IMB, d: adsorption of CP, e: adsorption of IMB

Conclusions

In this research, CNEF was successfully designed and optimized in Material studio 2017. Based on the adsorption of the drugs, encapsulating the CP was better and more possible due to its lower energy level, which is considered the spontaneous adsorption process.

Keywords

Adsorption, DFT, Molecular simulation, Drug delivery, CNT, Anti-cancer

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