台灣生醫材料重要推手-李昭仁教授簡介

李昭仁教授 (1935－1996)

- 台灣嘉義人，台大化工系畢業、美國奧克拉荷馬州立大學化工博士。
- 曾任職於清大工化系教授、系主任、工學院院長；專長於化工熱傳、生醫工程、材料與藥物制放之研究。
- 李教授曾獲**國科會傑出研究獎**、化工學會最高榮譽 -「**化學工程獎章**」；並致力於推展台灣醫工教育與研究，對台灣生醫工程的發展是重要的奠基者之一。
- 西元 1988 年成立「財團法人李昭仁教授生醫工程發展基金會」；設立**李昭仁教授生醫工程獎學金**，獎勵表現優秀的化工及生醫工程學生。
- 西元 2012 年設立「李昭仁教授生醫工程」**研究學者獎及生醫工程獎**。獎勵在生醫材料與藥物制放領域有傑出研究之學者及對上述領域之推廣、服務及教育具有優異貢獻之人士。

李教授昭仁博士，於西元 1935 年十月七日，生於台南縣善化鎮，係當時嘉義望族李外科診所著名外科醫師李博士連頂醫師令三郎，母親李陳銀杏為嘉義望族英安堂之五千金。

李教授一歲時，因父親任職彰化基督教醫院外科主任而舉家遷往彰化，後又遷往母親故鄉嘉義。六歲時進日治時代的嘉義玉川小學，直到二次大戰後，玉川國小改名為崇文國小，唸到五年級時即越級考上嘉義中學；六年中學成績皆名列前茅。西元 1953 年畢業後以第一志願考上台大化工系、成大電機系、師大工教系。當時李教授考取台大的成績可以進入台大醫科前十名，然而李教授並未報考醫科，成為其父母家人遺憾的一件事。但李教授並未後悔，進入化工系，開始專心致志於科技研究。西元 1961 年李教授在范良正教授指導下以論文 [Axial Density Distribution in Gas-Solid Fluidized Bed] 獲得堪薩斯州立大學碩士學位，同時準備繼續研讀博士學位。李教授接受主動提供助教獎學金的奧克拉荷馬州立大學，在 Dr. K.J. Bell 指導下研究熱傳，並於西元 1954 年，以論文 [A Theoretical and Experimental Investigation of the Leidenfrost Phenomena for Small Droplets] 獲得博士學位。同年六月開始任職於菲利浦石油公司。西元 1967 年應 Air Prod. Chem. 之邀請，到賓州該公司就職。兩年後因父親去世，即萌生回台心意。西元 1972 年李教授老友張昭鼎教授告知清大即將成立工學院，李教授於是欣然回台任教。

西元 1972 年至 1973 年間，毛高文教授任職系所主管時，李教授一年內將單操實驗室及化工課程等基礎工作逐步建立起來。西元 1973 年夏天毛高文所長離職後，由李教授接任系所主管，這期間李教授秉著大公無私及奮鬥不懈的精神，使所內各教職員心悅誠服共同努力，為工化系的發展努力。

西元 1979 年李教授擔任工化系所主管，六年任期期滿後，正值當時工學院院長林垂宙先生回美，請李教接替職務並擔任院長，李教授推辭，僅答應當代院長，第二年即由李卓顯先生接任；西元 1981 年時，毛高文先生回清大任校長，堅持請李教授當工學院院長，李教授盛情難卻之下，於西元 1981 年至西元 1984 年間繼續留在清大並任工學院院長，此後李教授一直不曾離開清大。在李教授擔任工學院院長的期間，完成了將工業化學系改名為化學工程學系外，並與高分子研究所合併成為化學工程學系暨研究所，成立工工所碩士班暨動機所、材料所、電機所博士班並招生；除此之外又成立生物工程中心並擔任中心主任，且積極與榮總合作研究推動榮清計畫至今。由於李教授豐沛的行政經驗及閱歷，往往為人所倚重，因而其後曾任工研院化工所顧問、財團法人自強工業技術服務社董事及執行長、生物工程中心主任、公害防治理事協會常務委員、教育部科技顧問室顧問、亞太科技協會理事、化工學會會誌總編輯、化工學會理事、中華民國醫學工程學會常務理事、中華民國生物力學學會常務理事暨中華民國生物力學理事等職務。

李教授回國時，即想到把所學的化學工程與醫學合併，而研究生醫工程，自己研讀一向生疏的人體生理學，二十多年來的努力成果卓著。早在西元 1975 年李教授即獲得工程論文獎，且由當時的行政院長蔣經國先生親自頒獎；後又於西元 1991 年獲得中國化學工程協會頒贈的化學工程獎章，並於西元 1993 年及 1995 年獲得國科會的傑出研究獎。而李教授更成為台灣生醫工程界的開山鼻祖，其大力提倡台灣的生醫工程發展，不斷的鼓勵後進成就今天台灣的生醫工程發展；而李教授亦不間斷的耕耘於研究上，至今在血液透析、人工代紅血球方面的研究無人能出其右，聞名於國際。李教授的努力成果頗受國際間學者的認可與賞識，因此在各國際學會李教授亦常被邀請為特別講座，如西元 1994 年在巴西舉行的生醫工程學會，李教授被邀請為特別講座，而西元 1996 年十月三日即去世前月，在日本全國人工臟器學會，李教授也是被邀請的兩位國際學者之一。其實當時李教授病情堪憂，然為了凸顯台灣生醫工程界的努力，李教授仍然抱病參加，而且前後講了一個多小時，聲音宏亮，內容豐富。同一年，李教授亦被國際知名的學

術期刊”Artificial Organ”十二月份雜誌做為封面人物，並獲聘為兩位榮譽客座編輯之一，惜李教授尚未來得及閱讀這一期的雜誌，便離開人世，非常遺憾。
李教授有傑出的語言能力，外語不只學得快也講得流利，很能表現出西方式的幽默，因此無論到美國、日本乃至德國，李教授總與人一見如故。因此當中日斷交後，李教授被指定為亞太科技協會的發起人，後並被選為理事及召集人之一，負責與日本亞東科技協會的交流達十年之久，各種活動都辦得有聲有色。

李教授與眾不同的是一生不求名利與世無爭，真正做到只做事不做官的精神，推辭了多次當主管的機會，西元 1978 年朱匯森先生當教育部長時，余傳韜先生極力推薦李教授當技職司長，並獲得部長同意，李教授卻婉拒了。醫工學會理事長的改選，也是相同的情形，李教授故意將自己票投給了對手，而使對方以一票之差當選。李教授自小聰明，常有先知之明，一切複雜事他往往能通盤瞭解，因此很快便能迎刃而解，達到事半功倍之效。但李教授為人謙虛，從不炫耀自己、標榜自己，研究論文雖然佳作連連，也不主動提出申請學術獎。李教授常說人人平等，比人聰明或地位高不值得驕傲，地位低也不必自貶。因此李教授待人一視同仁，自身全無官架。除了談公事開會，李教授絕不嚴肅，聚餐時李教授一定是大家的開心果。

「一粒麥子不落在地裡死了，仍舊是一粒；若是落地死了，就要生出許多粒子來。」相信李教授所遺留的典範、風度、信仰、必能繼續活在每個與其相處，受其感染的人。

(全文節錄自李昭仁教授紀念文集)

追思台灣生醫研發的開拓者－李昭仁教授

懷特生技新藥公司 鄭建新總經理

1979 年夏天當我從奧克拉荷馬州立大學化工系完成碩士學位，準備回台灣過暑假省親，我的論文口試委員之一，K. J. Bell 教授(他也是美國熱傳及熱力學的權威學者之一)給了我一個名字：C. J. Lee，要我回台灣時可去找他並代他致意問候。當時沒有 Google 搜尋工具及網路，加上回台時間短暫，這個任務一直沒有達成！直到 12 年後，我應時任工研院化工所胡德所長之聘，回國到化工所任職，進行釋放控制技術(Controlled Release Drug Delivery Systems)及經皮吸收貼劑產品開發，才與國內在這領域的開拓者李昭仁教授有較密切的交往，但當時絕沒想到李教授就是 Bell 教授口中的 C. J. Lee，因為我所認識的李昭仁是生醫領域的權威，怎麼會是傳統化工領域熱傳及熱力學的研究學者(後來才知道李教授是 K. J. Bell 很引以為傲的博士班學生)？這也讓我明白博士學位的獲得只是學習如何解決社會及工程問題的過程，而如何將這過程中獲得的知識和技能投入新領域的探討？才是一個學術研究者不斷引領學子創新突破的要素，從李昭仁教授的學術生涯具體形塑了成功典範。

我對李昭仁教授的另一個深刻印象是籌組「中華民國生醫材料及藥物制放學會」的過程，早在 1995 年之前即有相關領域學者專家提出籌組該學會的呼聲，因國內向來都有學者個別前往參加 Controlled Release Society 及 World Biomaterials Congress 年會並發表論文，深感必須整合大家力量，積極融入國際社群，為台灣正開始萌芽中的新興學術及產業領域發聲。我還記得最早的學會組織章程草案就在李昭仁教授辦公室討論出來的，第一次籌備會議也在清大化工館的教室舉行，並由李教授擔任主席，由於李教授深感國內要健全的發展生醫新領域，一定要結合學術界、法人研究單位、產業界及醫界的人才共同努力才能成功，學生畢業後也才有出路，因此雖然名稱為學會也堅持理監事必須納入這些專業領域的代表。但遺憾的後來因李教授罹患重病，學會的籌組也因此中斷了兩年多，直到 1998 年才在薛敬和教授大力推動下正式成立，實現了李教授的遺願。

時光荏苒，李教授離開我們匆匆已 20 年了，這 20 年來台灣生醫學術及產業的發展實在不可同日而語，許多年輕學者嶄露頭角，研究論文受到國際肯定；好幾家生技公司以藥物制放或生醫材料為核心平台技術，產品已陸續取得藥證上市，嘉惠患者，在資本市場也獲得投資者普遍認同；相信李教授在天之靈必會相當欣慰當年的辛勤播種，已逐漸在台灣這塊他所熱愛的土地上開花結果！

March 24 (Thu)				
18:30—20:30	Welcome Reception (Miramar Hotel Hsinchu)			
March 25 (Fri)				
8:00—8:30	Registration			
8:30—9:00	Opening Ceremony (Room B18)			
9:00—9:30	Plenary Lecture - Prof. Abraham Lee (Room B18)			
9:30—9:50	Coffee Break & Group Photo			
	Room B18 International Symposium on Theronostic Nanomedicine	**Room 209** Cross-strait DDS Symposium (A)	**Room 210** Cross-strait DDS Symposium (B)	**Room 202** Young Investigators and Students Competition
9:50—12:00	Oral Session 1			Biomaterials/ Tissue Engineering (Students)
12:00—13:00	BCRS Member Meeting	Lunch & Poster Session		
13:00—13:30	BCRS Board Meeting			
13:30—15:30	Oral Session 2			Drug Delivery (Young Investigators)
15:30—15:50	Coffee Break			
15:50—17:50	Oral Session 3			Biomaterials/ Tissue Engineering (Young Investigators)
18:30—20:30	Conference Banquet (Pengyuan Restaurant)			
May 26 (Sat)				
	Room B18 International Symposium on Theronostic Nanomedicine	**Room 209** Cross-strait DDS Symposium (A)	**Room 210** Cross-strait DDS Symposium (B)	**Room 202** Young Investigators and Students Competition
8:30—10:00	Oral Session 4			Drug Delivery (Students)
10:00—10:20	Coffee Break			
10:20—12:00	Oral Session 5			Drug Delivery (Students)
12:00—13:00	Lunch			
13:00—14:30	Oral Session 6			-
14:45—15:00	Closing Remarks (Room B18)			

藥物制放 (年輕學者)

3 月 25 日 (五) 13:30～15:30

編號	時間	題目	發表者
YOC-1	13:30～13:42	Active Targeted Nanoparticles for the Delivery of Epigallocatechin-3-Gallate in Cancer Therapy	林宥欣
YOC-2	13:42～13:54	Integrated self-assembling drug delivery system possessing dual responsive and active targeting for orthotopic ovarian cancer theranostics	王子威
YOC-3	13:54～14:06	Development of RGD-HA-modified gelatin nanoparticles with epigallocatechin gallate (EGCG) loading as Eye Drop for Corneal Neovascularization Treatment	曾靖孋
YOC-4	14:06～14:18	Fully Embeddable Polymer Microneedles as a Patch-Free Transdermal Drug Delivery System	陳美瑾
YOC-5	14:18～14:30	Gelatin Methacrylate/Carboxybetaine Methac-rylate Hydrogels with Tunable Crosslinking for Controlled Drug Release	游佳欣
YOC-6	14:30～14:42	Nanoscale combination treatment targeting resistance mechanisms associated with cancer therapy	陳韻晶
YOC-7	14:42～14:54	The Penetrated Delivery of Drug and Energy to Tumors by Nano-Composites	胡尚秀
YOC-8	14:54～15:06	Multifunctional Bubble Carriers for Oral Protein Drug Delivery	莊爾元

生醫材料/組織工程 (年輕學者)

3 月 25 日 (五) 15:50～17:50

編號	時間	題目	發表者
YOB-1	15:50～16:02	Adipose-Derived Stem Cells Enhance Burn Wound Healing and Neuropathic Pain Treatment	王惠民
YOB-2	16:02～16:14	Bioinspired Zwitterionic Surface Coatings with Robust Photostability and Fouling Resistance	黃俊仁
YOB-3	16:14～16:26	Blood Vessel Tissue Engineering: Combination of Endothelial Progenitor Cells, Extracellular Matrix and Aligned Electrospun Polyhydroxyalkanoate Scaffold	姚少凌
YOB-4	16:26～16:38	Cross-Linked Amniotic Membrane for Limbal Epithelial Stem Cell Niche Engineering	賴瑞陽
YOB-5	16:38～16:50	New Concepts in Synthesis and Characterization of Biomedical-Relevant Nanomaterials: a Combination of Colloidal- and Aerosol-based Approaches	蔡德豪
YOB-6	16:50～17:02	Functionalized Silk Thin Films with Gold Nanoparticles as Ultrahigh Broadband Absorber	萬德輝
YOB-7	17:02～17:14	Functionalized Graphene Oxide Nanosubstrates for Efficient Capture of Cells	陳冠宇
YOB-8	17:14～17:26	Nanogenerators for Self-Powered Sensing Applications	林宗宏
YOB-9	17:26～17:38	Multimodality Noninvasive Imaging for Assessing Therapeutic Effects of Exogenously Transplanted Cell Aggregates Capable of Angiogenesis on Acute Myocardial Infarction	黃玠誠

生醫材料/組織工程 (學生組)

3 月 25 日 (五) 09:50～12:00

編號	時間	題目	發表者
OB-1	09:50～10:02	Simultaneously Controlled Release of Doxorubicin and Indocyanine Green from Light-Triggerable Polymer Microneedles for Cancer Therapy	蘇良晟
OB-2	10:02～10:14	Electrostatic-directed assembly of nanosheet graphene oxide with silver and titania nanoparticles using dimensional, microscopic, and spectroscopic characterization	阮泰方
OB-3	10:14～10:26	Controlled Synthesis of Se-Supported Au/Pd Nanoparticles with Photo-Assisted Electrocatalytic Activity and their Application in Self-Powered Sensing Systems	張庭維
OB-4	10:26～10:38	Relationships between Surface Roughness/Stiffness of Chitosan Coatings and Fabrication of Corneal Keratocyte Spheroids: Effect of Degree of Deacetylation	李志鴻
OB-5	10:38～10:50	Evaluation of Silver Nanoparticles the Treatment of Bacterial Keratitis: Particle Shape Effect	林姿妤
OB-6	10:50～11:02	Fe@Au Core-Shell Nanoparticles for Thermotherapy and Drug Control Release	古煥暄
OB-7	11:02～11:14	Inflammation-Induced Drug Release by Using a pH-Responsive Gas-Generating Hollow-Microsphere System for the Treatment of Osteomyelitis	萬瑋琳
OB-8	11:14～11:26	Refilling Drug Delivery Depots form Mesoporous DNA/SPIONs System for Nanotherapeutic Drug Delivery in Deep Tumor Therapy	許語宸

藥物制放 (學生組 1)

3 月 26 日 (六) 08:30～10:00

編號	時間	題目	發表者
OC-1	08:30～08:42	A New Strategy of Microsphere Drug Delivery for Liver Cancer Treatment	湯哲宇
OC-2	08:42～08:54	Combination of Optimized Ligand Density and Magnetic Localization in Multifunctional Nanomedicine for Tumor therapy	江智聖
OC-3	08:54～09:06	Size-changeable Graphene Quantum Dot Nanotransformers for Penetrated Drug Delivery and Photothermal Therapy	蘇昱璘
OC-4	09:06～09:18	Remotely Triggerable Microneedle as a Programmable Transdermal Delivery System for Analgesic Agents	楊軒愷
OC-5	09:18～09:30	Dependence of Delivery Performance and Antiglaucoma Efficacy of Antioxidant-Functionalized Intracameral Pilocarpine Carriers on Grafting Amount of Gallic Acid	羅麗娟
OC-6	09:30～09:42	Core−Shell Structure, Biodegradation of Mixed Micelles of Atactic-PHB-mPEG and Isotactic-PHB-mPEG for Drug Delivery Systems	孫晧峰
OC-7	09:42～09:54	Photo-induced thermal-responsive nanogels for controlled drug release	張睿

藥物制放 (學生組 2)

3 月 26 日 (六) 10:20～12:00

編號	時間	題目	發表者
OC-8	10:20～10:32	Development of Photosensitive Polymer/Gold Nanocomplexes for drug/gene delivery and Stem Cells-based Therapy	莊鈞喬
OC-9	10:32～10:44	Targeting effect of decorated SN38-loaded liposomes on MCF-7 cell line	吳怡諄
OC-10	10:44～10:56	A Novel Bupivacaine Emulsion for Postoperative Pain	胡濬文
OC-11	10:56～11:08	Tumor-targeted nanoparticles co-deliver multi-inhibitors to overcome sorafenib-driven paradoxical activation of RAF/MEK/ERK pathway in hepatocellular carcinoma	劉亞琪
OC-12	11:08～11:20	Biodegradable Polymer/SPIO Nanocomplexes for Efficient Magnetofection, Magnetic Resonance Imaging and Anti-Cancer Therapy	黃日揚
OC-13	11:20～11:32	Porous Lipids@Silica/Carbon Nanosheets with Magnetic Stimulation in Enhanced Neural-like Cell Differentiation and Cancer Therapy	陳冠廷
OC-14	11:32～11:44	Multifunctional GCSF-Containing Nanoparticles for Oral Delivery to Chemotherapy-Induced Neutropenia Rat	林柏諺

生醫材料/組織工程

編號	題目	發表者
PB-1	Human Hair Keratin as a Template for Cell Adhesion and Adipose-derived Stem Cell Differentiation	蔡鎮宇
PB-2	Fixation of Fibronection on Aligned Electrospun Polyhydroxyalkanoate Scaffold Using Surface Modification Method for Vascular Tissue Engineering	林昶志
PB-3	Silver-Silica Hybrid Nanoparticles for Biomedical Applications	陳怡臻
PB-4	Kinetic Study of Ligand-Silver Nanoparticle Interactions to Colloidal Stability	張威昌
PB-5	Assembly of Functional Gold Nanoparticle on Silica Microsphere	汪軒蘭
PB-6	Gellan gum/Glucosamine films carrying 5-Chloro-8-hydroxy-7-iodoquinoline as an oral cancer treatment patch	黃奕鑾
PB-7	Understanding Ligand–Nanoparticle Interactions for Silica, Ceria, and Titania Nanopowders	賴彥志
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PB-18	Reduced Silver and Graphene Oxide-Based Nanoparticle-Containing Composites by Surface Graft Polymerization of Nano Silver and Graphene Oxide Containing Acrylic Acid	陳重杰
PB-19	Effect of Atmospheric Plasma Activate Surface and Graft Polymerization of NIPAAm Hydrogel on Deposition of Hydroapatite by Wet Process	鄭宜芸
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藥物制放

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PC-1	Development and Characterization of Swellable and Bioadhesive Gastroretentive Drug Dosage Form (sbGRDDF) Composed of Polyelectrolyte Hydrogel of Chitosan with ring-opened Polyvinyl Pyrrolidone (roPVP) for Improving Oral Bioavailability of Alendronate	蘇家妤
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PC-3	Preparation of albumin-bound nanoparticles by two steps emulsification	洪晟峰
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PC-5	PCOX Microneedles Containing Gelatin Microspheres as a Dual-Drug Release System for Transdermal Delivery of Hydrophilic and Lipophilic Drugs	陳佳穗
PC-6	Fabricating Multifunction PLGA NPs Reducing for Reperfusion Injury of MI Heart	林昇緯
PC-7	PLGA/SA Based Multifunctional NP/hBMSC Delivery System for Reducing Oxidative Injury of MI Heart	張峻翊
PC-8	Multitheranostic nanocapsule encapsulated with multiple drugs and Gd-neutron capture therapy facilitated by stem cell-magneto-based targeting for GBM	賴彥合
PC-9	Targeted Delivery of Functionalized Upconversion Nanoparticles for Near-Infrared Triggered Photothermal/Photodynamic Therapies of Orthotopic Glioblastoma	蔡源鍾
PC-10	Biodegradable in situ Gelling Polymers for the Treatment Dye Eye Disease	吳育銘
PC-11	Development of Drug-Eluting Intraocular Lens Improves Post-Cataract Surgical Complications	林庭萱
PC-12	Dual Stimuli-Responsive Chemodrug/Magnetite-Loaded Solid Lipid Nanoparticles for Enhanced Intracellular Drug Delivery and Effective Chemo-Thermal Therapy	劉得懿
PC-13	Dual-functional nanoparticles targeting CXCR4 and delivering anti-angiogenic siRNA ameliorate liver fibrosis	劉俊宏
PC-14	Microporous Coating Tablet as Oral Drug Delivery System with Constant Release	李元志

編號	題目	發表者
PC-15	Synergistic Combination Therapy Using a Core-Shell Lipid-Based Nanocapsule with Tunable Shell Thickness	許晉豪
PC-16	Preparation and Evaluation of Chrysin Loaded Polyketal Nanoparticles	張家錞
PC-17	Fabrication of Gelatin Covered Mesoporous Silica Nanoparticles as Sustained Release Drug Delivery System for Glaucoma Treatment	廖祐德
PC-18	Synthesis of inorganic nanoparticles/organic alginate composite for guiding chemotherapy of bladder cancer	陳薪元
PC-19	Encapsulation of low dosage propranolol by DSPC liposomes improved bone microarchitecture in ovariectomized rats	張栩榮
PC-20	ZnO-loaded Pluronic Nano-micelles for Tumor-targeting Drug Delivery System	林鴻儒
PC-21	A Nanoformulation of Antimicrobial Peptides and Anticancer Drugs in PEGylated Liposomes Inhibits Multidrug Resistance in Different Cancer Cells	駱雨利

口頭論文競賽

年輕學者組

YOC-1

Active Targeted Nanoparticles for the Delivery of Epigallocatechin-3-Gallate in Cancer Therapy

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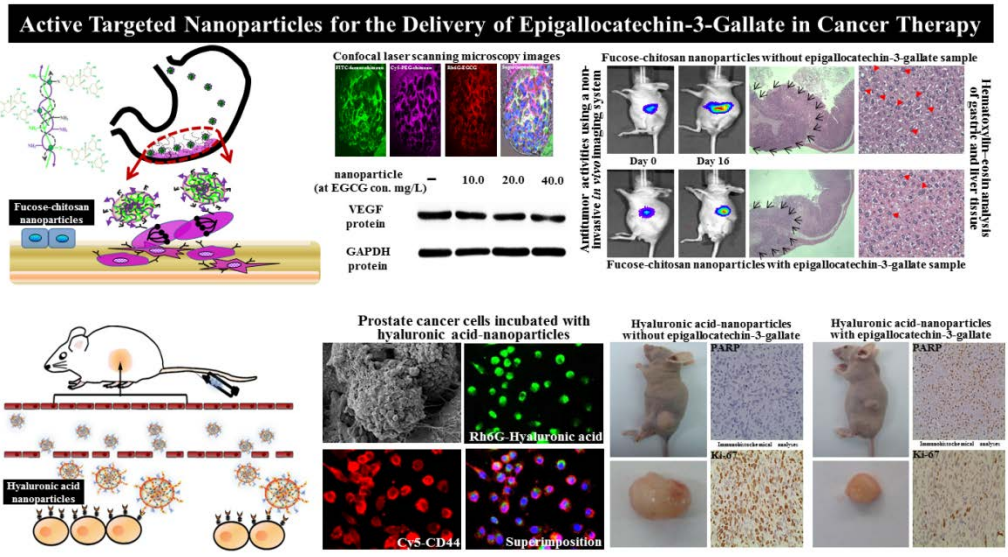
Green tea has been widely utilized for a long period of time and has diverse biological and pharmacological actions. Among tea catechins, (−)-epigallocatechin-3-gallate, a major constituent in the green tea polyphenol extract, has shown protection against inflammation or oxidative damage.[1] The green tea constituent epigallocatechin-3-gallate was found to inhibit matrix metalloproteinases that are intimately associated with tumor invasion and metastasis and has exhibited apoptosis-inducing activity of gastric and prostate cancers.[2] We evaluated a potential drug delivery system comprising the epigallocatechin-3-gallate entrapped within fucose-conjugated chitosan or hyaluronic acid nanoparticles, allowing topical administration of drug through a site-specific and target-activated release for oral treatment or intravenous injection of gastric or prostate carcinoma. The results show that the fucose-conjugated chitosan nanoparticles with pH-responsive characteristics can protect drugs from destruction by gastric acids, then significantly enhance the suppressive effect of epigallocatechin-3-gallate on gastric tumor growth and are effective in reducing gastric and liver inflammation in the orthotopic gastric tumor animal model. Meanwhile, we developed nanoparticles composed of hyaluronic acid and polyethylene glycol-gelatin of encapsulated epigallocatechin-3-gallate. The hyaluronic acid can make hydrogen bonds and van der Waals forces binding interactions with tumor cells through the CD44 molecule.[3] In *in vivo* experiment to verify the inhibition of prostate tumor growth after intravenous injection with nanoparticles and immunohistochemical analysis of tumor cell proliferation marker (Ki-67) and apoptotic marker [poly(ADP)ribose polymerase (PARP)] were performed on histological examination. Investigating these issues will improve nanoparticle combination with the addition of various chemotherapeutic agents and application to studies of clinical treatment.



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YOC-2

Integrated self-assembling drug delivery system possessing dual responsive and active ta rgeting for orthotopic ovarian cancer theranostics

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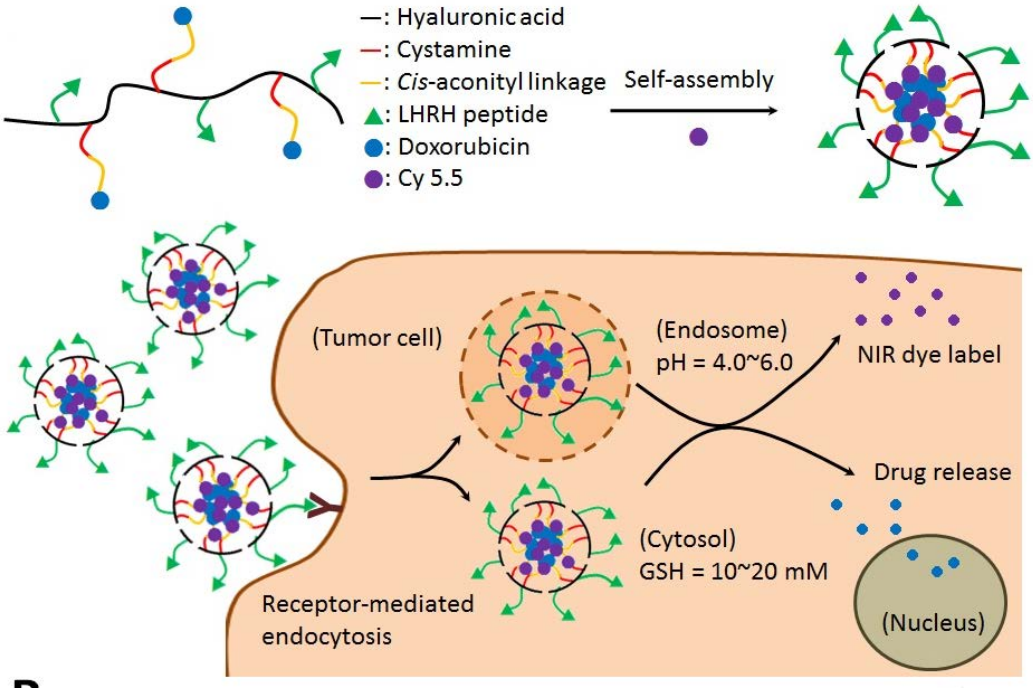
The purpose of this study is to develop a redox and pH-sensitive self-assembling hyaluronic acid nanoparticle with active targeting peptide for anticancer drug delivery. Anti-cancer drug is grafted onto hyaluronic acid (HA) via *cis*-aconityl linkage and disulfide bond to possess pH sensitivity and redox property, respectively. This conjugate is amphiphilic and can self-assemble into nanoparticle (NP) in aqueous solution. The results show that the nanoconjugate is successfully developed and the grafting ratio of cystamine (cys) is 17.8% with drug loading amount about 6.2% calculated by ^{1}H NMR spectra. The particle size is approximately 229.0 nm using dynamic light scatting measurement, and the morphology of nanoparticles is observed as spherical shape by transmission electron microscope. The pH and redox sensitivities are evaluated by changing either pH value or concentration of dithiothreitol in the medium. It is proved that the drug carrier is capable of achieving sustained controlled release of anti-cancer drug to 95% within 150 hours. The intracellular uptake is observed by fluorescent microscope and the images show that conjugating luteinizing hormone-releasing hormone (LHRH) peptide can enhance specific uptake of nanoparticles by OVCAR-3 cancer cells; thus, resulting in inhibitory cell growth to less than 20% in 72 hours *in vitro*. Orthotopic ovarian tumor model is also established to evaluate the therapeutic and diagnostic efficacy using non-invasive in vivo imaging system. The representative results demonstrate that LHRH-conjugated NPs possess a preferable tumor imaging capability and an excellent antitumor ability to almost 30% of original size in 20 days.



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YOC-3

Development of RGD-HA-modified gelatin nanoparticles with epigallocatechin gallate (EGCG) loading as Eye Drop for Corneal Neovascularization Treatment

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Normal cornea is transparent; neovascularization (NV) of cornea can disrupt visual function causing blindness. Finding a way to treat cornea NV is needed. In this study, we fabricated arginine-glycine-aspartic acid (RGD) peptide conjugated hyaluronic acid (HA), then coating on gelatin nanoparticles with epigalloccatechin-3-gallate (EGCG) loading (GEH-RGD) for targeting the αvβ3 integrin on vascular endothelia cells. The *in vitro* evaluations were tested by human umbilical vascular endothelia cells (HUVECs). A mouse model with alkaline burn to induce cornea NV for evaluate therapeutic effect of this nanomedicine delivered topically *in vivo* was evaluated. The GEH-RGD nanoparticles were successfully synthesized and its size was around 168.87 nm, with an EGCG-loading efficiency up to 95%. Cell viability test showed GEH-RGD could efficiently inhibit HUVECs viability at the EGCG concentration > 20 μg/ml. HUVECs migration ability was inhibited by the GEH-RGD nanoparticles. Moreover, cell invasion and tube formation assays shows that GEH-RGD had the most significant anti-angiogenesis effect on HUVEC compare with EGCG solution and non-RGD modified nanoparticles. Furthermore, MMP_2 and MMP_9 from HUVECs were suppressed in GEH-RGD treated group via zymography test. Data from the alkali burned mice model showed inhibition of vascular growth in the damage cornea treated by GEH-RGD, and less vascular ingrowth in the cornea was also found in histological section. Overall, we confirm that GEH-RGD nanoparticle was successfully developed and it can specific target to αvβ3 integrin as a vascular endothelium cells inhibited agent, and it's work for treating corneal NV mice with anti-angiogenesis effect. This nanomedicine, GEH-RGD, can be used as an eye-drop for the treatment of ocular NV in clinics in the future.

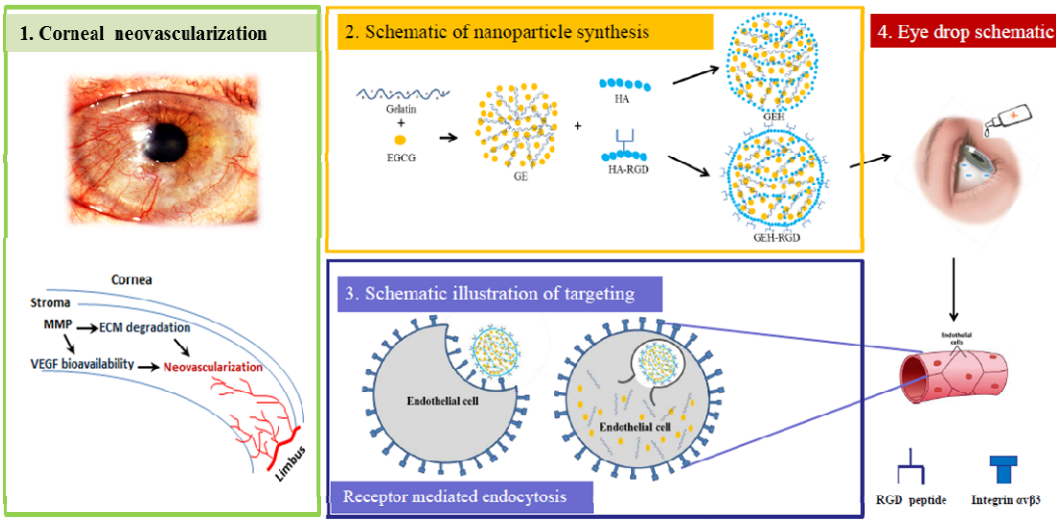

Fig. 1 Schematic illustration of GEH-RGD nanoparticles as eye drop for corneal NV treatment

YOC-4

Fully Embeddable Polymer Microneedles as a Patch-Free Transdermal Drug Delivery System

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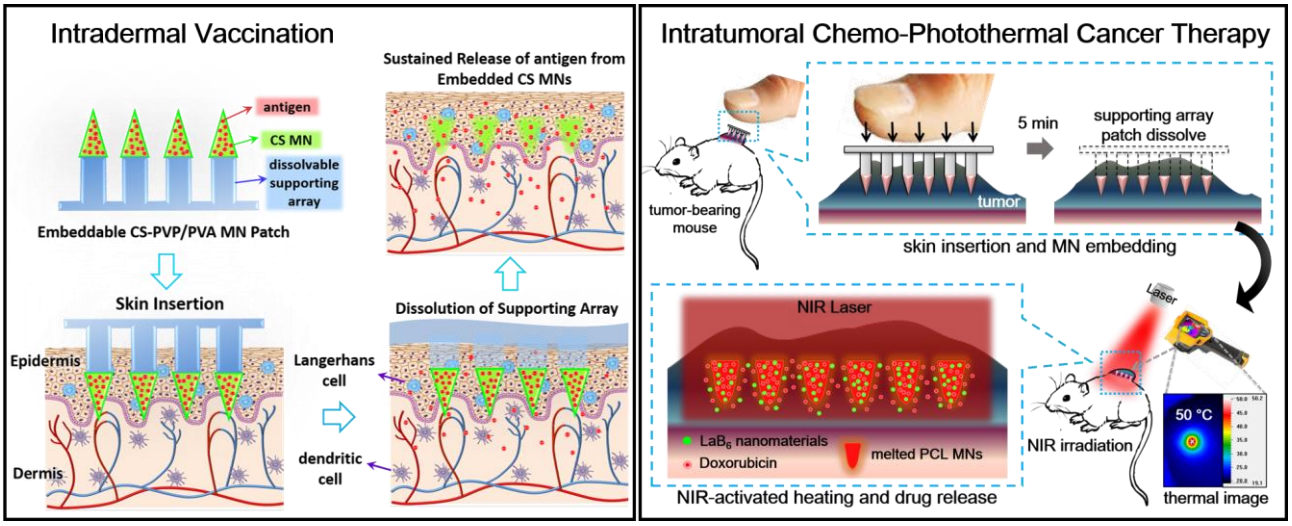
Incomplete insertion is a common problem associated with polymer microneedles (MNs) that results in a limited drug delivery efficiency and wastage of valuable medication. To address this problem, this talk introduces a fully insertable MN system with a dissolvable supporting structure design to ensure complete and efficient delivery of encapsulated payload. The supporting structure was connected to the base of the biodegradable MN. It provides mechanical strength and aids in overcoming skin deformation during skin puncture, thus enabling full insertion of the MN into the skin. When inserted into the skin, the supporting structures can be quickly dissolved in the skin within a few mins, thus embedding the MNs into the target tissue for sustained and locoregional drug delivery. Such design allows sustained delivery of drugs into the skin without needing to wear a patch, thus preventing uncomfortable feeling and skin irritation. We have developed three kinds of embeddable MNs for different clinical applications:

- **Chitosan MNs for intradermal vaccination**
- **Polycaprolactone MNs for intratumoral chemo-photothermal cancer therapy**
- **Hyaluronic acid MNs for intradermal delivery of dermal filler**

The embeddable MN system provides a more convenient, feasible, and patient-acceptable methodology than conventional one for transdermal administration of therapeutics.



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YOC-5

Gelatin Methacrylate/Carboxybetaine Methac-rylate Hydrogels with Tunable Crosslinkin g for Controlled Drug Release

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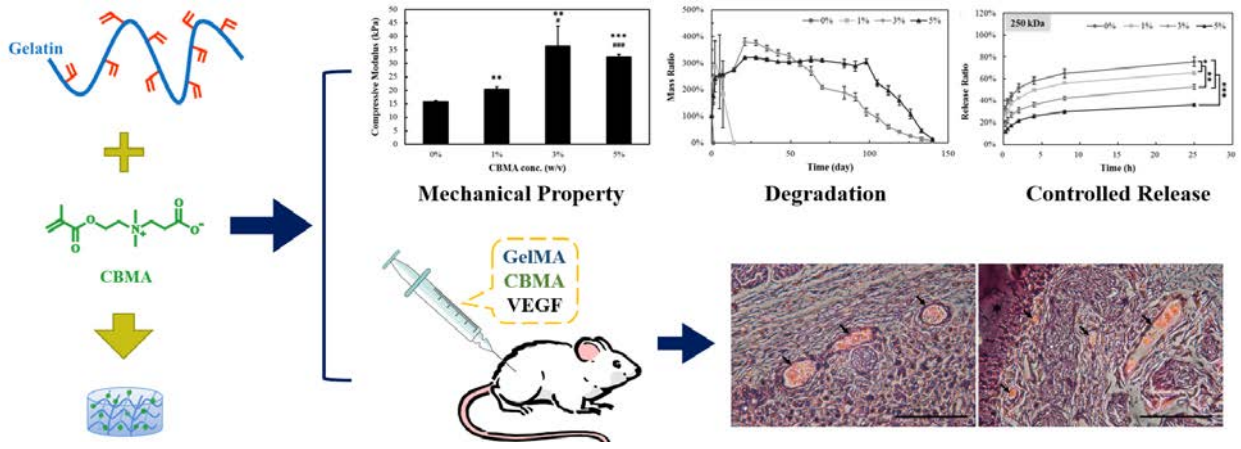
Gelatin-based hydrogels have been frequently used in drug releasing applications. Gelatin has not shown antigenity and can be completely resorbed in vivo, and has the physicochemical properties that can be suitably modulated.3 Many crosslinkers such as dialdehydes, carbodiimide, transglutaminase, and genipin have been utilized to fabricate chemically crosslinked gelatin hydrogels.4-6 In addition to these crosslinkers, methacrylated gelatin (GelMA) has also been used to prepare hydrogels by exposing to ultraviolet light3 or by redox reaction using ammonium persulfate (APS) and N, N, N', N'-tetramethylethylenediamine (TEMED). These methods can make the structure of hydrogels more homogeneous, since no additional crosslinkers are added.

In this work, methacrylated gelatin (GelMA) based hydrogels were fabricated with carboxybetaine methacrylate (CBMA) to manipulate the properties of the gelatin-based hydrogels, since CBMA is a much smaller compou nd than gelatin. With the incorporation of CBMA, these hydrogels demonstrated better mechanical property, sl ower degradation rate, and controlled drug release rate compared with GelMA alone group. GelMA/CBMA hy drogels also showed good cell viability. As in the in vivo test, vascular endothelial growth factor (VEGF)-loa ded GelMA/CBMA hydrogels displayed certain degrees of angiogenesis. These results indicate that GelMA/CB MA hydrogels are biocompatible, and the properties of GelMA/CBMA hydrogels can be easily tuned with the ratio of CBMA. These characteristics make GelMA/CBMA hydrogel a promising material for drug delivery a nd tissue engineering.



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YOC-6

Nanoscale combination treatment targeting resistance mechanisms associated with cancer therapy

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Molecularly targeted therapy against cell proliferation, angiogenesis and fibrosis has recently emerged as a highly promising therapeutic strategy for treating hepatocellular carcinoma (HCC). However, both intrinsic and acquired resistance to the targeted mono-therapy and unwanted toxicity often develop and restrict the therapeutic efficacy and clinical application of the treatment. Our aim is to develop tumor targeted nanoparticle (NP) formulation to specifically co-deliver multiple therapeutic siRNAs or small molecule drugs into HCC and thus target the compensatory activated pathway in the tumor cells and stromal cells in the microenvironment. To this end, the targeted multifunctional NPs can provide an effective approach for overcoming drug resistance, leading to better therapeutic effects in treating cancer.

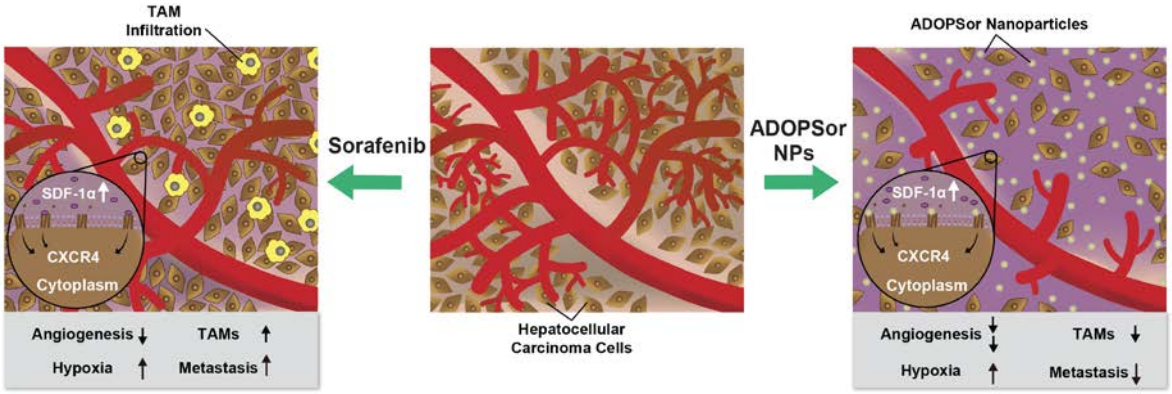

Figure: Sorafenib-loaded CXCR4-targeted NPs deliver sorafenib into HCCs, overcome stroma-mediated resistance to sorafenib, and achieve enhanced therapeutic effects in HCC.

YOC-7

The Penetrated Delivery of Drug and Energy to Tumors by Nano-Composites

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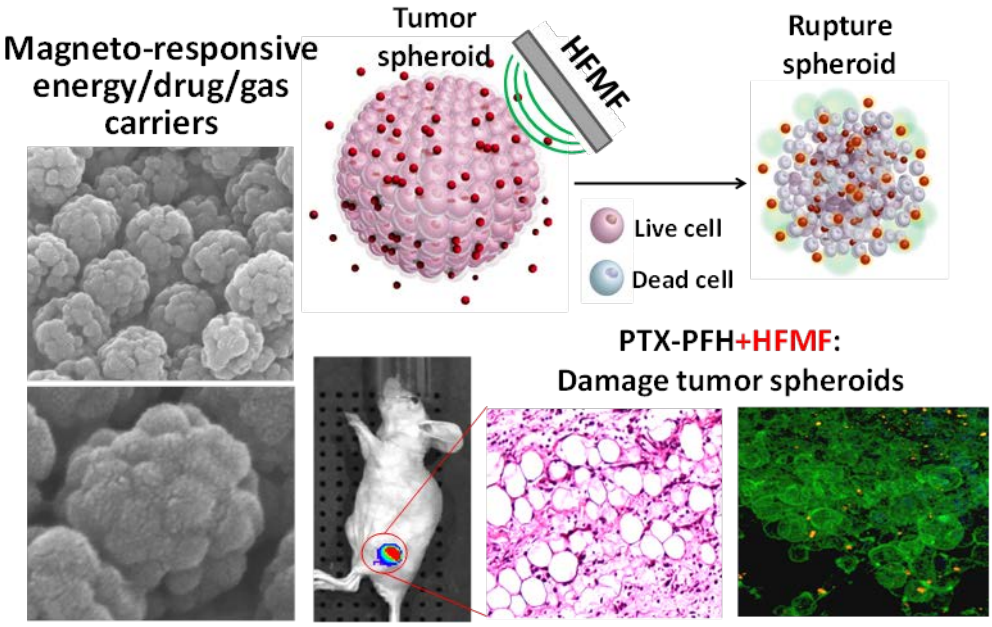
A responsive energy/drug carrier that enhances deep tumor penetration with a porous nano-composite is constructed by using a tumor-targeted lactoferrin (Lf) bio-gate as a cap on mesoporous iron oxide nanoparticles (MIONs). With a large payload of a gas-generated molecule, perfluorohexane (PFH), and a hydrophobic anti-cancer drug, paclitaxel (PTX), Lf-MIONs can simultaneously perform bursting gas generation and on-demand drug release upon high-frequency magnetic field (MF) exposure. Biocompatible PFH was chosen and encapsulated in MIONs due to its favorable phase transition temperature (56 °C) and its hydrophobicity. After a short-duration MF treatment induces heat generation, the local pressure increase via the gasifying of the PFH embedded in MION can substantially rupture the three-dimensional tumor spheroids *in vitro* as well as enhance drug and carrier penetration. As the MF treatment duration increases, Lf-MIONs entering the tumor spheroids provide an intense heat and burst-like drug release, leading to superior drug delivery and deep tumor thermo-chemo-therapy. With their high efficiency for targeting tumors, Lf-MIONs/PTX-PFH suppressed subcutaneous tumors in 16 days after a single MF exposure. This work presents the first study of using MF-induced PFH gasification as a deep tumor-penetrating agent for drug delivery.



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YOC-8

Multifunctional Bubble Carriers for Oral Protein Drug Delivery

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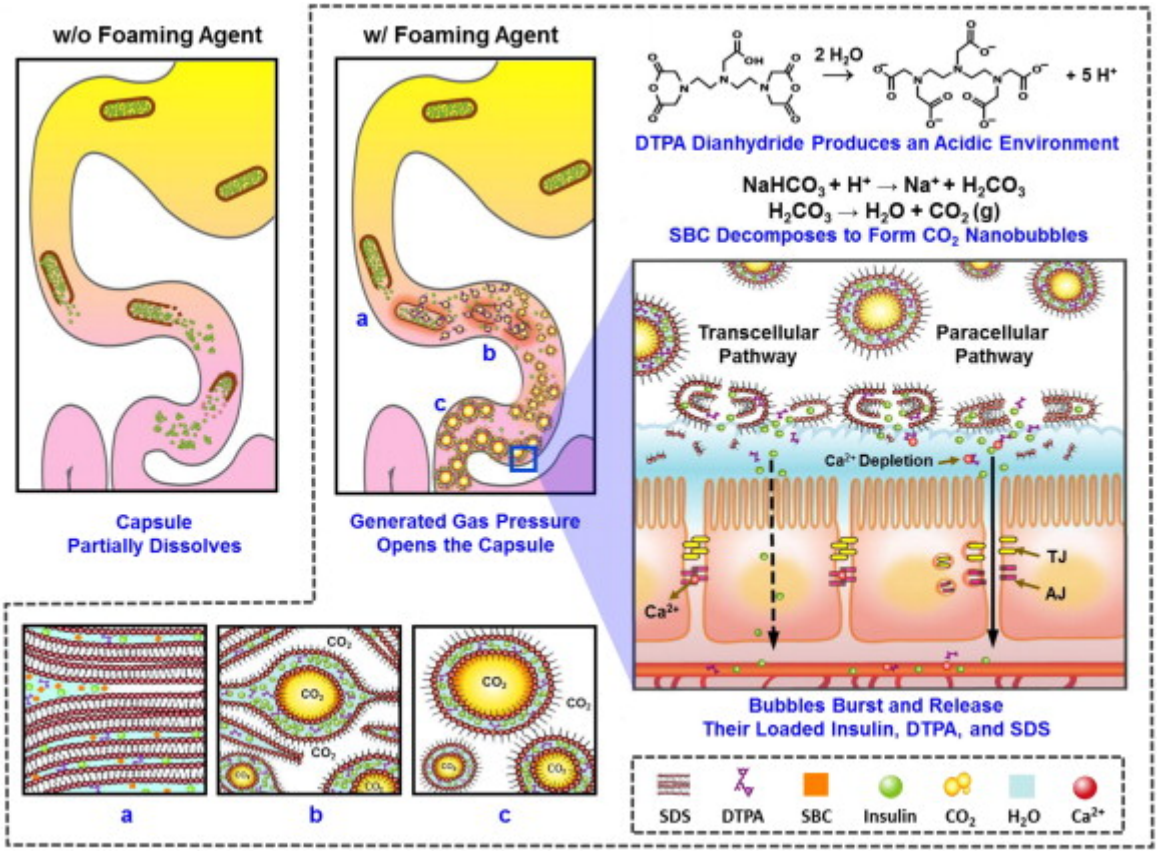
Successful oral delivery of therapeutic proteins such as insulin can greatly improve the quality of life of patients. This study develops a bubble carrier system by loading diethylene triamine pentaacetic acid (DTPA) dianhydride, a foaming agent (sodium bicarbonate; SBC), a surfactant (sodium dodecyl sulfate; SDS), and a protein drug (insulin) in an enteric-coated gelatin capsule. Following oral administration to diabetic rats, the intestinal fluid that has passed through the gelatin capsule saturates the mixture; concomitantly, DTPA dianhydride produces an acidic environment, while SBC decomposes to form CO2 bubbles at acidic pH. The gas bubbles grow among the surfactant molecules (SDS) owing to the expansion of the generated CO2. The walls of the CO2 bubbles consist of a self-assembled film of water that is in nanoscale and may serve as a colloidal carrier to transport insulin and DTPA. The grown gas bubbles continue to expand until they bump into the wall and burst, releasing their transported insulin, DTPA, and SDS into the mucosal layer. The released DTPA and SDS function as protease inhibitors to protect the insulin molecules as well as absorption enhancers to augment their epithelial permeability and eventual absorption into systemic circulation, exerting their hypoglycemic effects.



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YOB-1

Adipose-Derived Stem Cells Enhance Burn Wound Healing and Neuropathic Pain Treatment

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Stem cells are found in multi-cellular organisms, and are biological undifferentiated cells which can differentiate into specialized cells to divide and produce more stem cells through mitosis. In adult organisms, stem cells and progenitor cells act as a repair system for the body replenish adult tissues. We select to carry on the experiments with adipose-derived stromal/stem cells (ADSCs), because the obtaining on clinic is easy; the chance of surgery complication is low; the patient acceptance is high; the cultured cell number is in a large quantity; and the proliferative generation is stable. Burn injury has been shown to bring out the neuropathic pain in general cases, and it is hard to cure. The present clinical medicine is with low efficacy, and is often accompanied obvious side effects. The management of neuropathic pain after burn injury is a critical issue. We found that the over-inflammation and the neuron apoptosis in spinal cord ventral horn in burn damaged rat. ADSCs can be applied to diminish inflammation, decrease neuropathic pain and reduce neuron apoptosis. Following, we will move to treat the difficult wound (high glucose conditions). During normal wound healing, various kinds of cells are recruited to the wound by cytokines released from the injury area. The prolong inflammation and the poor circulating / resident cell migration impaired the diabetic wound healing. The elevated TNF-□ expression decreases fibroblast proliferation and increases apoptosis of fibroblast. The local injection around the wound with keratinocyte-secreted cutaneous T-cell attracting chemokine (CTACK) is shown to improve wound healing by recruiting circulating cells. In our clinical preliminary data, the increased TNF-□ expression with the decreased CTACK expression was noted in diabetic wound fluids compared with the normal wound fluids. This will be a worth topic to discuss the relationships between ADSCs and the wound repair.

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YOB-2

Bioinspired Zwitterionic Surface Coatings with Robust Photostability and Fouling Resistance

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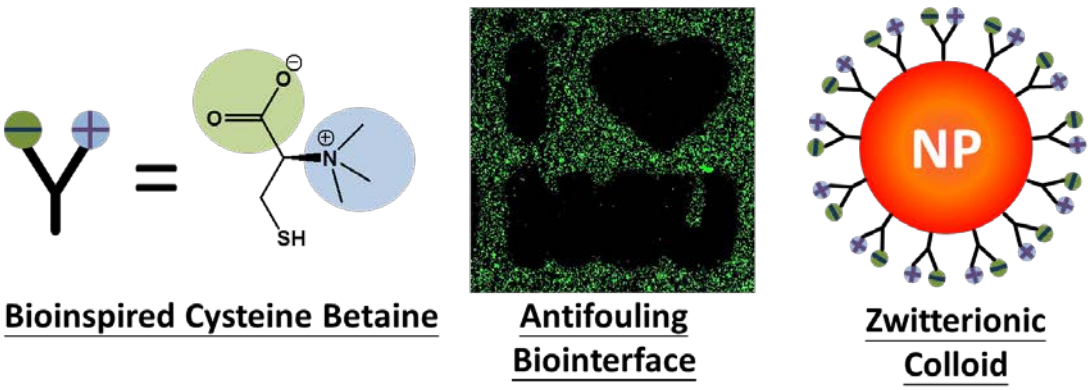
Great care has been paid to the biointerface between a bulk material and the biological environment, which plays a key role in optimized performance of medical devices. In this work, we report a new superhydrophilic adsorbate, called L-cysteine betaine (Cys-b), having branched zwitterionic groups that give rise to surfaces and nanoparticles with enhanced chemical stability, biofouling resistance, and inertness to environmental changes. Cys-b was synthesized from the amphoteric sulfur-containing amino acid, L-cysteine (Cys), by quaternization of its amino group. Gold surfaces modified with Cys-b exhibited prominent repellence against the nonspecific adsorption of proteins, bacteria, and fibroblast cells. In addition, Cys-b existed in zwitterionic form over a wide pH range (i.e., pH 3.4 to 10.8), and showed excellent suppression in photo-induced oxidation on gold substrates. Furthermore, the modification of hollow Ag@Au nanoshells with Cys-b gave rise to nanoparticles with excellent colloidal stability and resistance to coordinative interaction with Cu^{2+}. Taken together, the unique features of Cys-b offer a new nanoscale coating for use in a wide spectrum of applications.



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YOB-3

Blood Vessel Tissue Engineering: Combination of Endothelial Progenitor Cells, Extracellular Matrix and Aligned Electrospun Polyhydroxyalkanoate Scaffold

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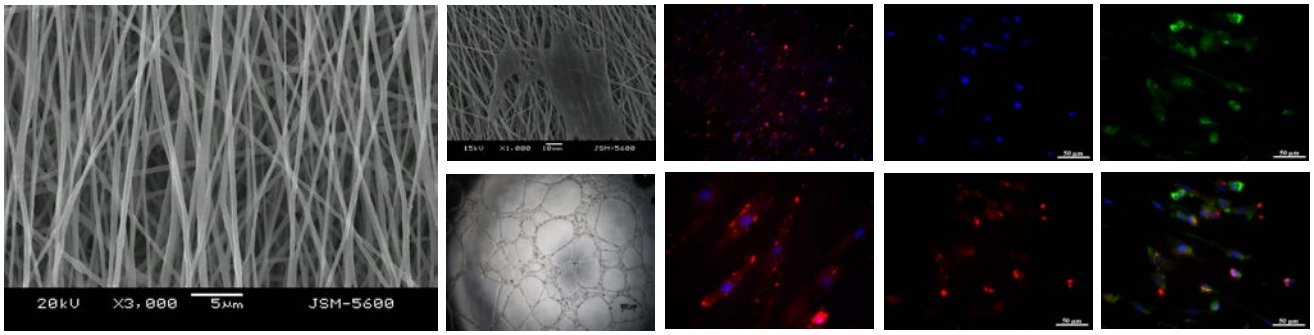
Repair and regeneration of vascular tissue is the important research topic of current biomedical engineering and regenerative Medicine. Many studies indicated that cells need to grow on the suitable extracellular matrix to show the particular functionality. In this study, we tested various surface modification methods to fix fibronectin or collagen on the biodegradable polymer surface (poly(3-hydroxybutyrate, PHB and poly(3-hydroxybutyrate-co-3-hydroxyvalerate), PHBV). Then, the cell lines (3T3 and L929) and primary cells (endothelial progenitor cells, EPCs and human umbilical vein endothelial cells, HUVECs) were cultured on the modified surface to explore the application potential of vascular tissue engineering. Our data showed that the surface of alignment PHB and PHBV films can be modified successfully by chemical methods based on Ninhydrin assay and contact angle assay. XPS assay also confirmed ECM has immobilized on the film. In addition, the WST1 assay, immunocytochemistry assay and SEM showed that the surface modified films performed excellent cell compatibility. The cells cultured on the surface modified films, the cell viable assay showed that the films had good biocompatibility. Taken together, our results demonstrated that PHB and PHBV films that were modified by the above chemical method and were fixed with suitable ECM can provide a potential artificial vessel for application of vascular tissue engineering.

EPCs on Fibronectin Coating Aligned Electrospun PHBV Scaffold



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YOB-4

Cross-Linked Amniotic Membrane for Limbal Epithelial Stem Cell Niche Engineering

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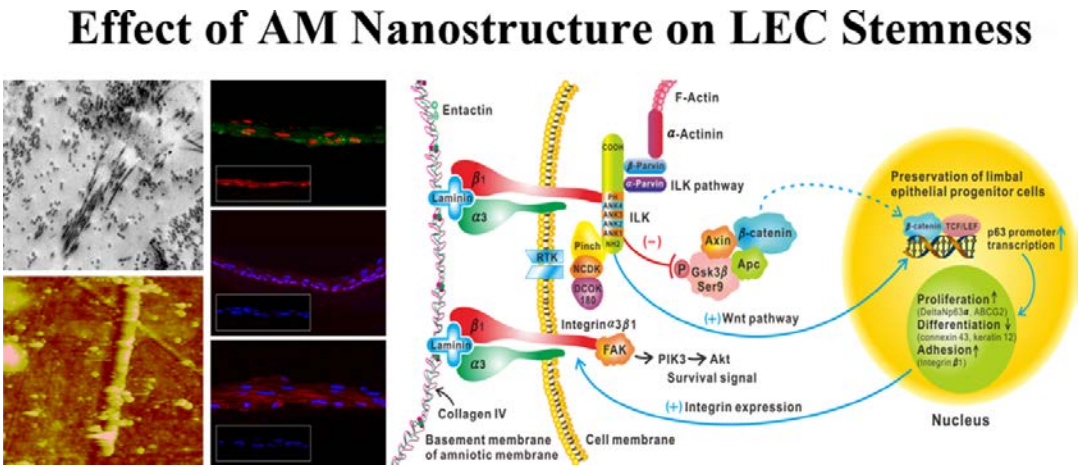
Amniotic membrane (AM) is one of the most prevalent natural matrices used for ophthalmic tissue engineering. To overcome the poor biostability of tissue matrix, this study aims to develop physically or chemically modified AM material for limbal stem cell niche. Our results show that although the photo-cross-linking does not cause potential harm, a major problem with this technique is the difficulty in increasing molecular cross-linking density of AM collagen. Because of the high reactivity of cross-linking agent, glutaraldehyde-treated biological tissues are detrimental to the cultured human corneal epithelial cells, in particular for the case of high cross-linking degree. In contrast, water-soluble carbodiimide is found to be a preferable chemical cross-linker for stabilization of AM matrices because it can induce biomaterial cross-linking without taking part in the linkages. The cross-linker-mediated nanoscale change in collagen fibrous structure induces substantial alteration of chemically modified biological tissues. Marked increases in light transmittance, resistance to enzymatic degradation, and cell stemness are noted for samples with a greater extent of cross-linking. Since protein denaturation occurs upon carbodiimide treatment, the biophysical cue may play an important role in regulating limbal epithelial cell (LEC)-biomaterial interaction. Our findings also suggest that the LEC stemness enhancement is highly correlated with Wnt signaling pathway. Mild to moderate pretreatment conditions (i.e., 3-10 mM L-lysine) can provide a useful strategy to assist in the stabilization of carbodiimide cross-linked AM tissue scaffolds. In conclusion, carbodiimide-based cross-linking treatment represents a potential AM biomaterial processing method in development of an artificial corneal epithelial stem cell niche.



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YOB-5

New Concepts in Synthesis and Characterization of Biomedical-Relevant Nanomaterials: a Combination of Colloidal- and Aerosol-based Approaches

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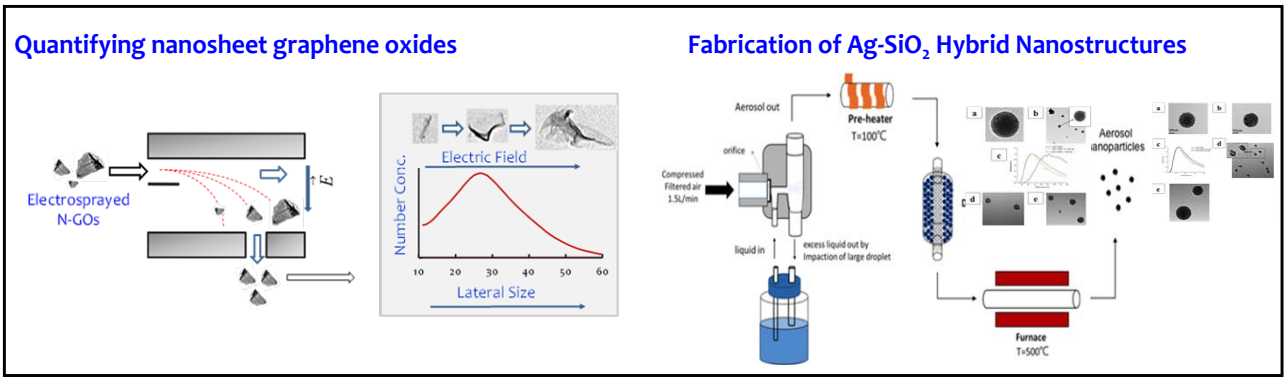
We present a systematic study on the developments of biomedical-relevant functional nanomaterials from the prospects of materials synthesis and characterization. For nanomaterial characterization, electrospray-differential mobility analysis is employed to study dis-assembly/de-aggregation of metal organic framework, quantification of nanosheet graphene oxide colloids, protein-silver nanoparticle interactions, ligand–nanoparticle interactions for silica, ceria, and titania nanopowders, and orthogonal analysis of functional gold nanoparticles for biomedical applications. Physical size and colloidal stability of nanomaterials are tunable by the adjustment of environmental conditions. Complementary physical, microscopic and spectroscopic characterization methods are incorporated to the study, allowing for a concept of applications of nanomaterial colloids involving the control of particle size and homogeneity and further proving the capability of in-situ semi-quantitative analysis in a variety of aqueous formulations.

For nanomaterial synthesis, we create different functionalities via molecular conjugation on the surface of nanomaterials, including the controlled formation of dithiothreitol-conjugated gold nanoparticle clusters and assembly of nanosheet graphene oxide with silver and titania nanoparticles. A systematic controlled synthesis of the construct of gold nanoparticle on silica microsphere is developed using an electrostatic-directed approach, by which we can effectively improve the homogeneity and the loading of gold nanoparticles on silica microsphere for application in liver cancer therapy. A gas-phase approach is established to fabricate silver-silica hybrid nanostructure, where the surface plasmonic resonance of silver colloids can be enhanced significantly. Our work provides a generic way to implement the design of fabricating functional nanomaterials through a well-controlled synthetic route for emerging biomedical applications (e.g., hyperthermal therapy, targeted drug delivery).



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YOB-6

Functionalized Silk Thin Films with Gold Nanoparticles as Ultrahigh Broadband Absorber

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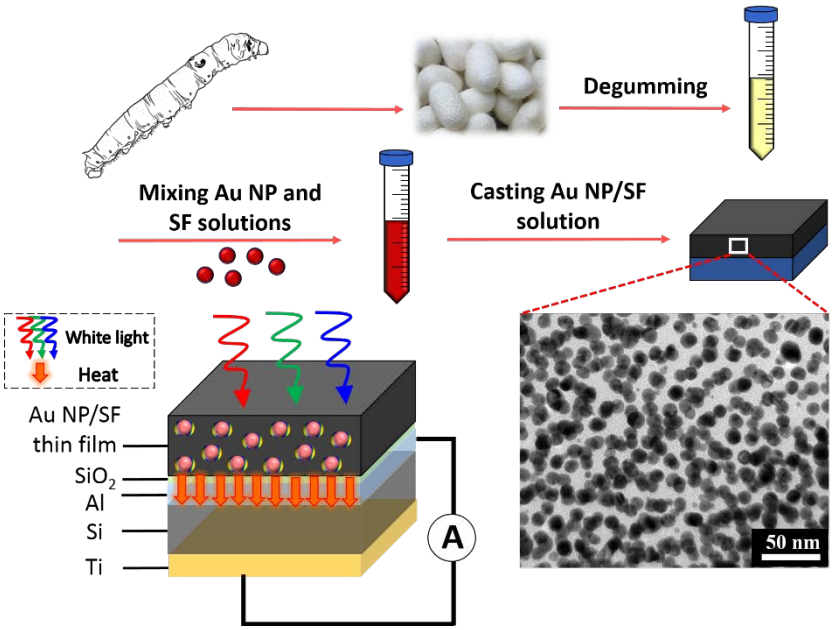
In this study, the phenomenon of white-light-induced heating in silk fibroin (SF) films embedded with gold nanoparticles (Au NPs) is systematically investigated. As far as we are aware, this study is the first to employ Au NPs to develop an ultrahigh broadband absorber and also the first to use a white light source for the photothermal generation. By increasing the Au content in the composite films, the absorbance could be enhanced significantly around the localized surface plasmon resonance (LSPR) wavelength and also raised dramatically at the non-LSPR wavelengths. The optimized composite film exhibits an ultrahigh absorbance of ca. 95% over a wide spectral range of 350-750 nm, and moderate absorbance values in the longer wavelength range of 750-1000 nm (e.g., ca. 60% at 1000 nm). Therefore, significant temperature increases on the order of ca. 100°C could be readily obtained when the composite film is irradiated by a LED or a halogen lamp. In this case, the composite film could absorb almost all of the incident light and accordingly convert the optical energy to local heat. Moreover, the composite films also display a linear light-to-heat response with light intensity and a great photothermal stability. Finally, the broadband absorptive film is coated on a Al/Si Schottky device and displays a linear, significant, stable photo-thermo-electronic response with varying light intensity.



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YOB-7

Functionalized Graphene Oxide Nanosubstrates for Efficient Capture of Cells

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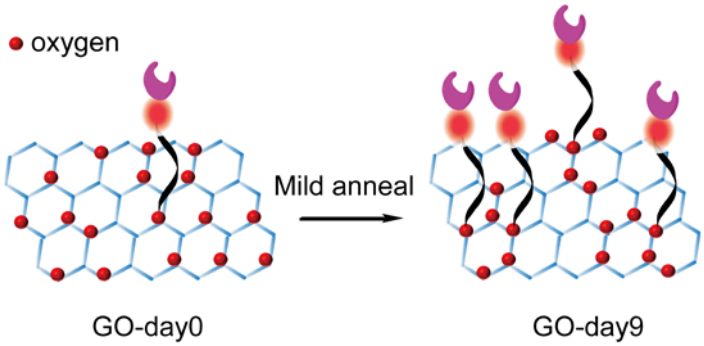
Graphene oxide (GO) has attracted significant interest as a template material for multiple applications due to its two-dimensional nature and established functionalization chemistries. Currently, as-synthesized GO nanosheets are employed directly to this end with no structural modifications. Here, we induce a phase transformation (oxygen clustering) in GO and demonstrate its benefits for one such application – biomolecule detection. We utilize the modified form of GO to construct a highly sensitive and planar device that allows for quick and efficient capture of murine class-II MHC+ cells. Our approach leads to a capture efficiency of ~92% at room temperature, remarkably higher than the efficiency afforded by devices using as-synthesized GO directly, ~54%. We show that the enhanced efficiency stems from improved functionalization of GO with antibodies as a result of chemical changes induced by oxygen clustering in GO. Overall, our work highlights a general route to improve functionalization of GO for various applications..



Schematic showing the functionalization scheme to graft antibodies onto the GO thin films

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YOB-8

Nanogenerators for Self-Powered Sensing Applications

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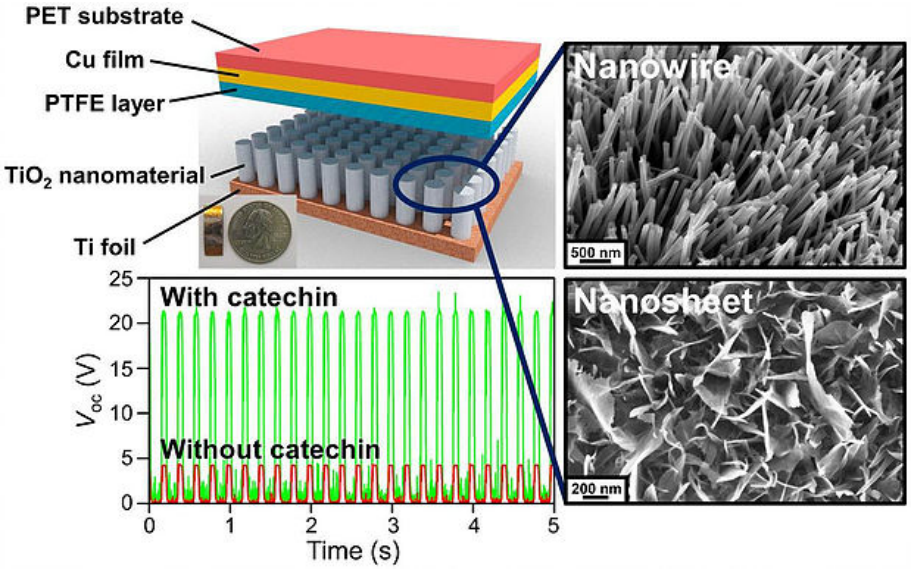
Self-powered nanosensors that can function without external power sources have recently been demonstrated as new approaches for various sensing targets. By harvesting energy directly from the human body to power biomedical devices, these self-powered sensors and systems are advantageous in minimizing the size, having long-term operation (little maintenance), and avoiding the use of environmentally unfriendly materials in battery. Since the first invention of triboelectric nanogenerator (TENG) in 2012, it has been developed into a new energy technology for self-powered sensing application. TENG has been applied to efficiently convert the human motions into electricity. The fundamental mechanism of the TENG is based on surface charge transfer, which is through the contact between two materials with different triboelectric polarity. The serial contact and separation of the material surfaces with opposite charges establishes a potential difference, which will drive the electrons flow through the external load. Because the capability of surface charge transfer depends on the physical and chemical properties of the surfaces, in this research we further functionalize the material surface for selective detection of different targets. The self-powered nanosensors developed here are also future sensing system for unreachable and access-denied extreme environments.



The example of using self-powered nanosensor for catechin molecule detection

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YOB-9

Multimodality Noninvasive Imaging for Assessing Therapeutic Effects of Exogenously Transplanted Cell Aggregates Capable of Angiogenesis on Acute Myocardial Infarction

Chieh-Cheng Huang[1], Hao-Ji Wei[2], Kun-Ju Lin[3], Wei-Wen Lin[4], Hsin-Yi Hu[1], Po-Ming Chen[1], Meng-Hsuan Hsieh[1], Yen Chang[*2], Hsing-Wen Sung[*1,5]

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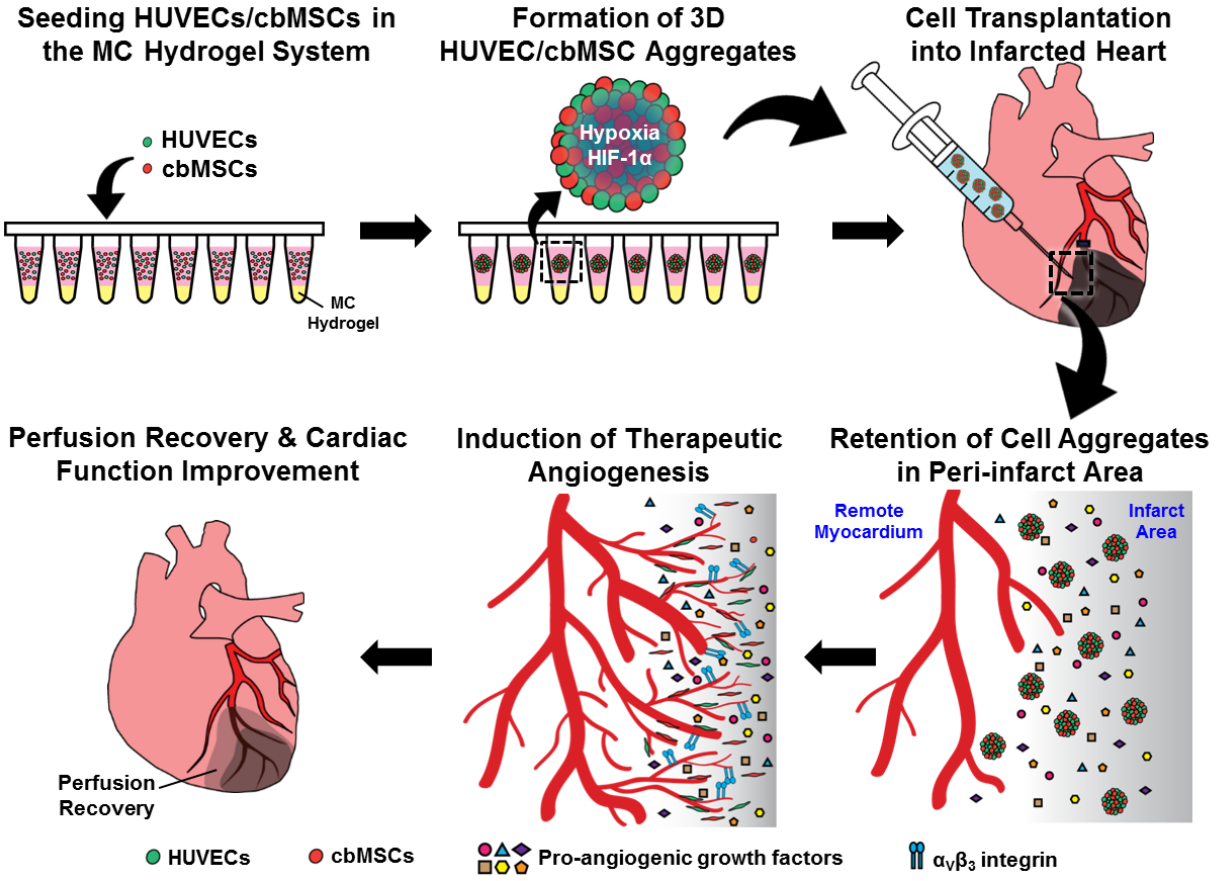
Although the induction of neovascularization by cell-based approaches has demonstrated substantial potential in treating myocardial infarction (MI), the process of cell-mediated angiogenesis and its correlation with therapeutic mechanisms of cardiac repair remain elusive. In this work, three-dimensional (3D) aggregates of human umbilical vein endothelial cells (HUVECs) and cord-blood mesenchymal stem cells (cbMSCs) are constructed using a methylcellulose hydrogel system. By maximizing cell-cell and cell-ECM communications and establishing a hypoxic microenvironment in their inner cores, these cell aggregates are capable of forming widespread tubular networks together with the angiogenic marker $\alpha_v\beta_3$ integrin; they secret multiple pro-angiogenic, pro-survival, and mobilizing factors when grown on Matrigel. The aggregates of HUVECs/cbMSCs are exogenously engrafted into the peri-infarct zones of rats with MI via direct local injection. Multimodality noninvasive imaging techniques, including positron emission tomography, single photon emission computed tomography, and echocardiography, are employed to monitor serially the beneficial effects of cell therapy on angiogenesis, blood perfusion, and global/regional ventricular function, respectively. The myocardial perfusion is correlated with ventricular contractility, demonstrating that the recovery of blood perfusion helps to restore regional cardiac function, leading to the improvement in global ventricular performance. These experimental data reveal the efficacy of the exogenous transplantation of 3D cell aggregates after MI and elucidate the mechanism of cell-mediated therapeutic angiogenesis for cardiac repair.



口頭論文競賽

學生組

OB-1

Simultaneously Controlled Release of Doxorubicin and Indocyanine Green from Light-Triggerable Polymer Microneedles for Cancer Therapy

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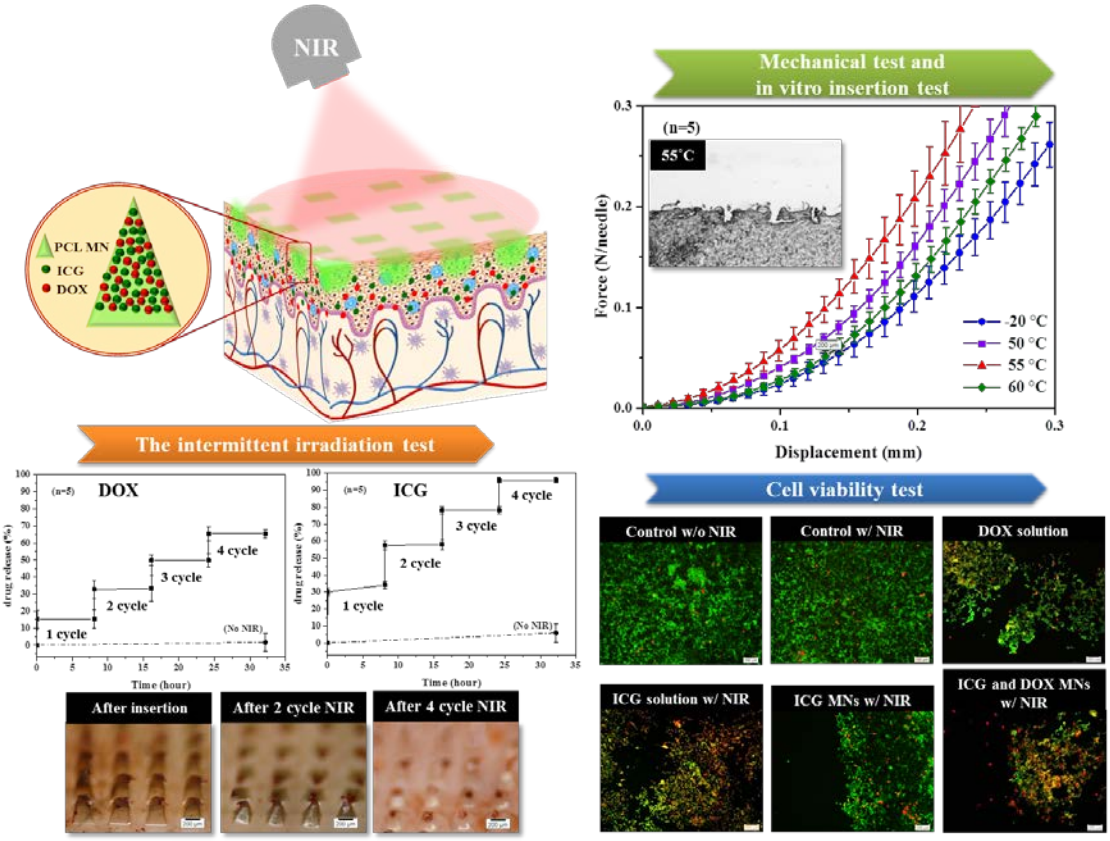
In this study, we developed doxorubicin (DOX) and indocyanine green (ICG)-loaded near-infrared (NIR) light-triggerable polymer microneedles (MN) for synergistic photodynamic (PDT), photothermal (PTT), and chemotherapy. ICG can produce single oxygen and heat after absorbing NIR light, thus expanding its utility for PDT and PTT for cancer therapy. To improve MN's mechanical strength, MN was recrystallized at 55 °C for 24 h. The heat treated MNs can be inserted into porcine skin at a depth of 191 ± 12 μm. When irradiated with NIR, the ICG transduced the light energy to generate heat, thus causing the MN melting at 48 °C. This increased the mobility of the polymer chain, enabling simultaneous release of DOX and ICG from the MNs. Drug release can be switched on and off at least 4 cycles, and a consistent dose was delivered in each cycle with high reproducibility. DOX/ICG-loaded MNs in combination with laser irradiation caused significantly higher cytotoxicity than that caused by the administration of a free single drug as well as ICG-loaded MNs in breast cancer cells. Simultaneous administration of PDT, PTT and DOX from MNs is a powerful approach for the ablation of malignant cells and can be extended to treat superficial cancers.



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OB-2

Electrostatic-directed assembly of nanosheet graphene oxide with silver and titania nanoparticles using dimensional, microscopic, and spectroscopic characterization

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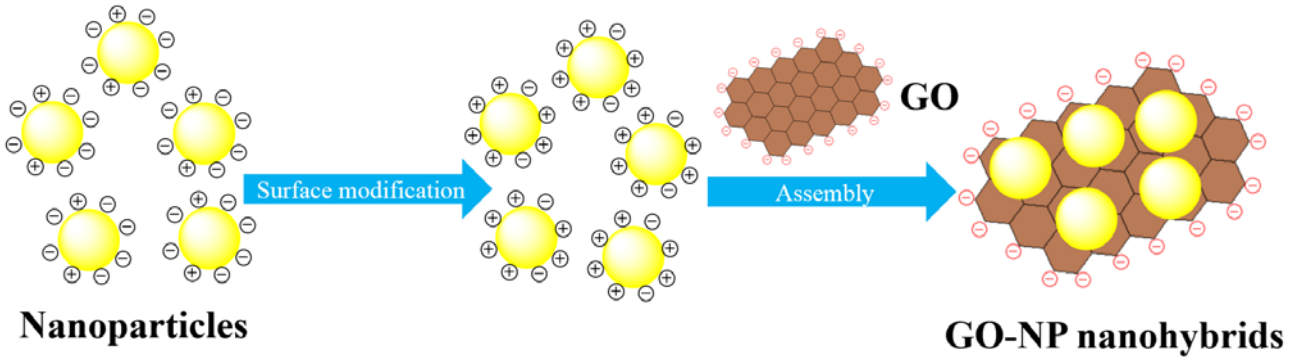
ABSTRACT: We present a synthetic approach for the fabrication of graphene oxide (GO)-based nanohybrids using an electrostatic-directed assembly. Materials properties, such as particle size distribution, number concentration, colloidal stability, surface charge, and morphology of GO-based nanohybrids, were characterized complementarily by electrospray-differential mobility analysis, transmission electron microscopy, X-ray photoelectron spectroscopy, and zeta potential analysis. The results show the GOs are able to combine with Ag nanoparticle and titania nanoparticle to form the nanohybrids of GO-AgNP and GO-TiO_2-NP, respectively. The colloidal stability of nanohybrids can be optimized through the control of relative number concentrations. Our study demonstrates a prototype approach to fabricate GO-based nanohybrids in the aqueous phase by design. The work also provides an effective method to characterize GO-based nanohybrids, which can be used to optimize the performance in the fields of targeted drug delivery, antibacterial activity, and photo-degradation.

Key words: graphene, titania, silver, nanohybrids



OB-3

Controlled Synthesis of Se-Supported Au/Pd Nanoparticles with Photo-Assisted Electrocatalytic Activity and their Application in Self-Powered Sensing Systems

Ting-Wei Chang[1], Chia-Wei Wang[2], Chuan-Hua Chen[1], Chia-Lun Hsu[2], Huan-Tsung Chang[2] and Zong-Hong Lin*[1]

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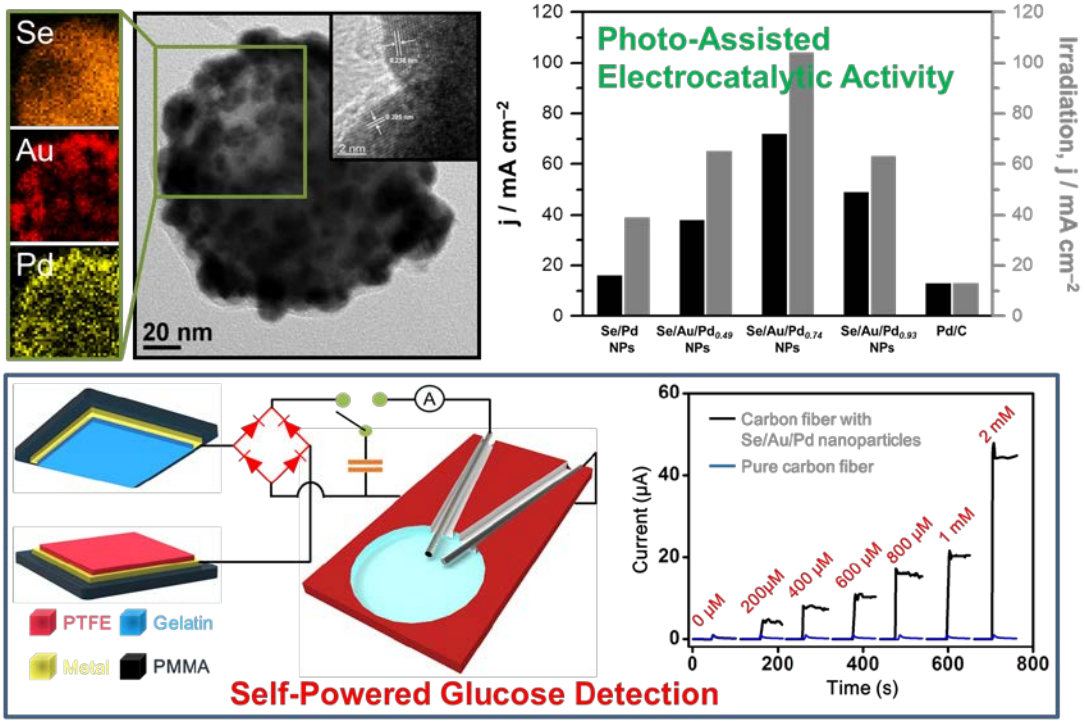
Bimetallic nanoparticles (NPs) have received increasing attention for their outstanding catalytic activity which the corresponding monometallic NPs can hardly achieve. In this paper, we developed a facile approach to prepare Se-supported Au/Pd NPs with high and photo-assisted electrocatalytic activity. Cyclic voltammetry (CV) measurements showed that the electrocatalytic activity of the Se-supported Au/Pd NPs was dependent on the Pd content. This result indicates that the interface between Pd and Au plays a vital factor in the electrocatalytic activity, while the individual metal components in the Se/Au/Pd system are of minor relevance for such activity. The Se-supported Au/Pd NPs exhibited mass activities of 4.25 (A/mg_{Pd}) and 1.21 (A/mg_{Au+Pd}) toward ethanol oxidation, which were higher than that of the commercial Pd/C catalyst (0.36 A/mg_{Pd}). The electrocatalytic activity of Se-supported Au/Pd NPs was further enhanced by 2.4 times under solar light irradiation due to the photoelectrochemical effect of the Se NPs. It was further demonstrated in this paper that the presence of Se-supported Au/Pd NPs is crucial in self-powered electrochemical sensing systems as the overall sensitivity is significantly improved.



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OB-4

Relationships between Surface Roughness/Stiffness of Chitosan Coatings and Fabrication of Corneal Keratocyte Spheroids: Effect of Degree of Deacetylation

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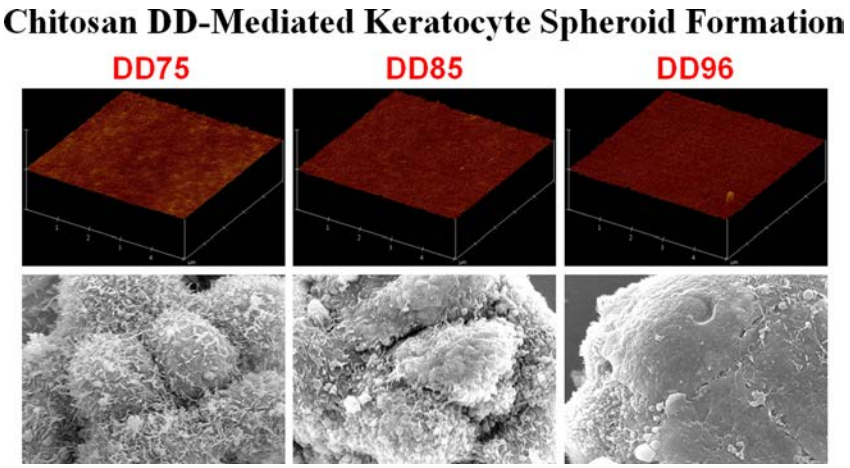
Cell spheroid fabrication has important implications to the advance in tissue engineering while stimulation from interface of a biopolymer coating has the ability to modulate this event. This study aims to investigate the dependence of keratocyte migration, proliferation, and differentiation on surface roughness/stiffness of chitosan coatings through modifications by degree of deacetylation (DD). Chitosan coatings with increasing DD exhibited significantly decreased surface roughness and increased surface stiffness. During in vitro cultivation, the relationships between the behaviors of rabbit corneal keratocytes (RCKs) and biopolymer coatings with varying DDs (between 75% and 96%) were found. Both the surface roughness increase and stiffness decrease led to enhanced cell migration, which is the main driving force for the early stage spheroid formation on chitosan substrates (e.g., within 8 h). With these stimulations from substrates, the size and morphology of RCK spheroids were greatly affected by DD of chitosan. When fabricated on a lowered DD of chitosan material, the spheroids had a larger size with abundant extracellular matrix production. At a later stage of spheroid cultivation (e.g., 5 days), significantly higher amount of RCKs on chitosan coatings was noted with increasing DD, indicating the interface effects on cell proliferation. The keratocan expression of RCK spheroids grown on a lowered DD of chitosan was up-regulated, suggesting that both surface roughness increase and stiffness decrease may facilitate the microenvironment for preservation of cellular phenotype. Overall, our work contributes to the scientific understanding of keratocyte behaviors and spheroid fabrications in response to DD-mediated surface roughness/stiffness of chitosan coatings.



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OB-5

Evaluation of Silver Nanoparticles the Treatment of Bacterial Keratitis: Particle Shape Effect

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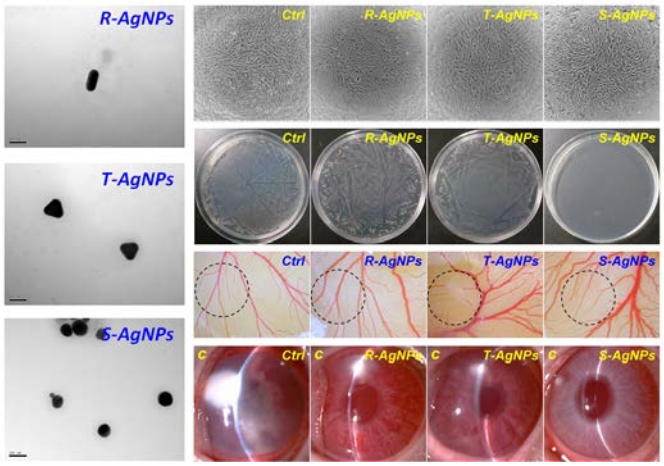
Bacterial keratitis is a severe eye condition that is caused by pathogen infection. Topical application of antibiotic is currently the common way to treat bacterial keratitis. However, this administration would affect the effectiveness of drug action. In addition, abuse derived from multi-drug resistant strains of the gene and cannot be exempted from the dilemma of corneal neovascularization. Therefore, in order to overcome the above mentioned defect of the current treatment modality, the development of nanomaterials with antibacterial and anti-angiogenic ability, and repair of corneal tissue. Today, the nanotechnology on biomaterials is the trends, thus the selection with a good antibacterial material - silver as a research base was expect to assess treatment of bacterial keratitis through different shapes. In this study, preparation of silver nanoparticles with rod-shaped, triangular flakes and the spherical, and the exclusion of consideration of the effect of the surface area of the particles carried geometric design, experiments and found that through the interaction of different shapes of silver nanoparticles with cells, bacteria action has been a marked difference. Furthermore, we found the treatment of bacterial keratitis animal model via silver nanoparticles significantly improved symptoms which effectively reduce the bacteria, corneal inflammation and edema, and complications with blocking angiogenesis. Our findings suggest that it concluded that the spherical nanoparticles is the best therapeutic agent among other groups.

Schematic of AgNPs for Treatment on Bacterial Keratitis



OB-6

Fe@Au Core-Shell Nanoparticles for Thermotherapy and Drug Control Release

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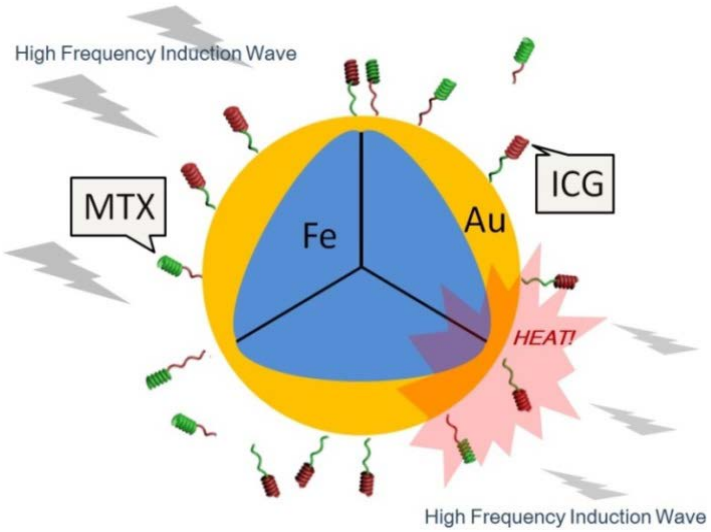
This study was to prepare Fe@Au core-shell nanoparticles (Fe@Au) by microemulsion methods. The products were grafted with the anticancer drug methorexate (MTX) to become multifunctional magnetic nanocomposites applying to magnetic resonance imaging, magnetic guiding, magnetic hyperthermia treatment and drug control release. Specific textured structure was further fabricated onto the nanoparticles to enhance optical properties. The crystalline structure was determined using XRD to verify the phases of iron and gold. The molar ratio of Fe to Au was 1:1 through EDS analyzed. According to the results of SQUID tests, the Fe@Au nanoparticles were superparamagnetic at room temperature and the saturated magnetization were 29 emu/g under 10000 Oe. A high-frequency wave generator was used to test the magnetic hyperthermia property. The temperature of 10 mg/mL Fe@Au solution was increased from room temperature to 48.5^{o}C in 20 minutes. Results of *in vitro* test showed that a dose below 500 μg/mL was not cytotoxic to L929 cell. The UV-VIS spectra presented an absorption peak at 310 nm, which confirmed the successful surface grafting of MTX. For the textured Fe@Au core-shell nanoparticles (tFe@Au), they presented a cobble stone shape with specific ridges through TEM and SEM observation. The molar ratio of Fe to Au was 1:3 through EDX analysis. The results of UV-VIS spectroscopy showed that tFe@Au had absorption peaks at 540 nm, and between 750 nm and 800 nm. We conclude that the magnetic nanocomposites are able to be applied for cancer hyperthermia treatment.



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OB-7

Inflammation-Induced Drug Release by Using a pH-Responsive Gas-Generating Hollow-Microsphere System for the Treatment of Osteomyelitis

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In the conventional treatment of osteomyelitis, the penetration of antibiotics into the infected bone is commonly poor. To ensure that the local antibiotic concentration is adequate, this work develops an injectable calcium phosphate (CP) cement in which is embedded pH-responsive hollow microspheres (HMs) that can control the release of a drug according to the local pH. The HMs are fabricated using a microfluidic device, with a shell of poly(D,L-lactic-co-glycolic acid) (PLGA) and an aqueous core that contains vancomycin (Van) and NaHCO3. At neutral pH, the CP/HM cement elutes a negligible concentration of the drug. In an acidic environment, the NaHCO3 that is encapsulated in the HMs reacts with the acid rapidly to generate CO2 bubbles, disrupting the PLGA shells and thereby releasing Van locally in excess of a therapeutic threshold. The feasibility of using this CP/HM cement to treat osteomyelitis is studied using a rabbit model. Analytical results reveal that the CP/HM cement provides highly effective local antibacterial activity. Histological examination further verifies the efficacy of the treatment by the CP/HM cement. The above findings suggest that the CP/HM cement is a highly efficient system for the local delivery of antibiotics in the treatment of osteomyelitis.

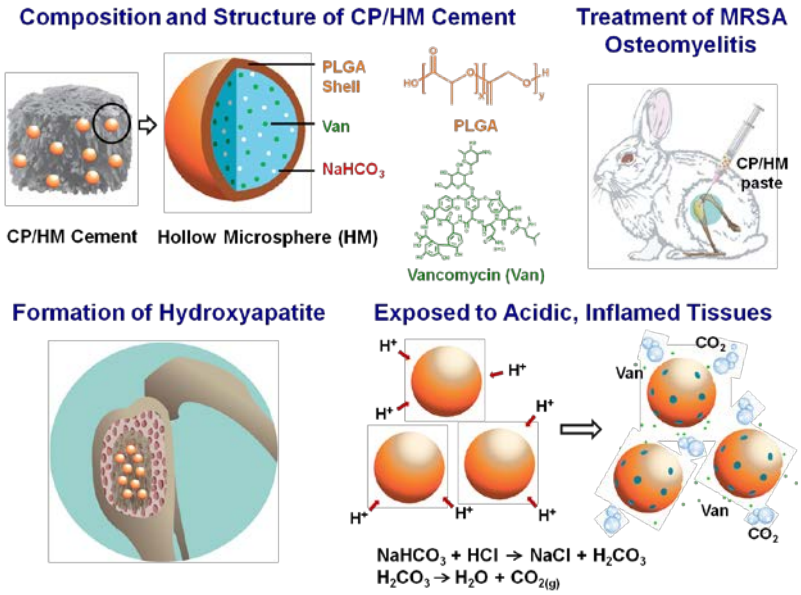

Figure 1. Schematic illustrations showing the composition and structure of injectable CP/HM composite cement developed in the study and its mechanism in treatment of osteomyelitis.

OB-8

Refilling Drug Delivery Depots form Mesoporous DNA/SPIONs System for Nanotherapeutic Drug Delivery in Deep Tumor Therapy

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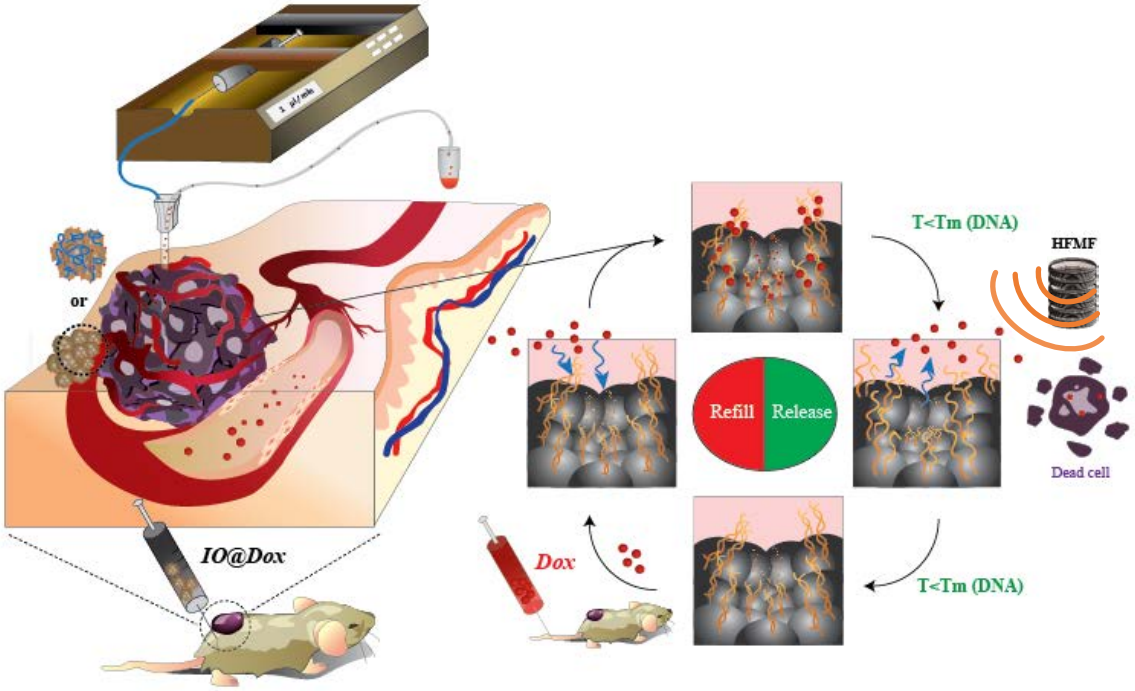
We invented the new type of refilling drug device made up of mesoporous superparamagnetic iron oxide nano particles (MP-SPION), whose particles diameter is less than 200 nm, which leads to a significantly increased EPR effect and enhanced antitumor drug effects as well, and its surface is coated with oleylamine (OAm) wer e conjugated via their 5' ends to double DNA strand. Utilizing the ability of DNA strandsbind Doxorubicin (Dox) reaching drug toxicity in tumor cell. Additionally, injection of Dox could repeatedly refill an intratumor DNA-conjugated MP-SPIONs device and inhibited tumor growth better than controls reliant on the EPR effect alone.

Here we demonstrate that DNA-conjugated MP-SPIONs drug payloads can be used for refilling of Dox and t hat this concept can be exploited for tumor treatment. It was hypothesized that device refilling with drug c ould be mediated by melting temperature of DNA strands, nucleic acids have been implemented asstimuli-respo nsive on the surface associated with MP-SPIONs, Dox is release from a high temperature below DNA melting temperature, and adsorption of Dox in a low temperature above DNA melting temperature as a duplex stru ctures. Control the temperature of DNA strands on the MP-SPIONs, and dru-g infused into the blood of a pat ient extravasate into target tissues and are bound by the nanodevice where accumulation in tumor site by e xternal magnetic attraction, subsequently allowing for sustained rel-ease of drug at the target site. High-frequen cy magnetic field (HFMF) capable of generate heat is appliedto DNAstrand local controlled drug release, In s ummary, an ideal system for localized drug delivery wo-uld allowfor minimally invasive refilling of drug depo ts for repeat drug dosing over the course of days or weeks.



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OC-1

A New Strategy of Microsphere Drug Delivery for Liver Cancer Treatment

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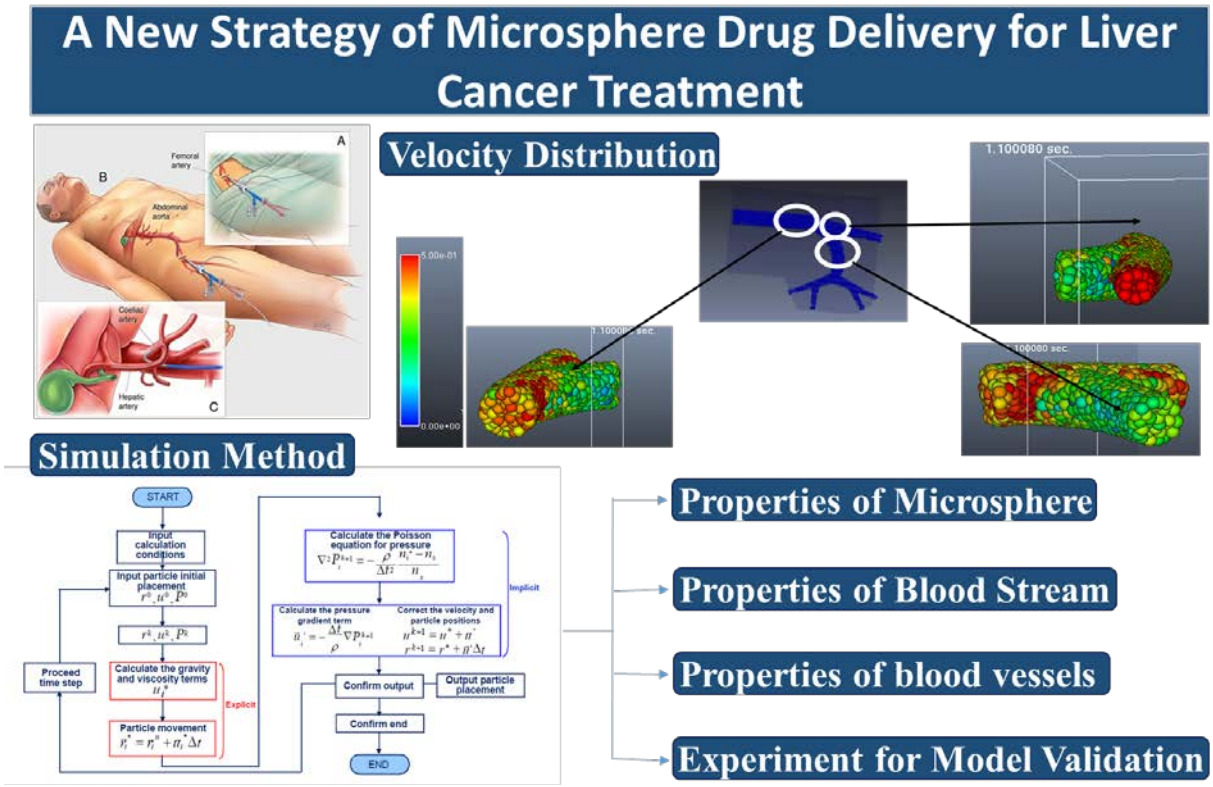
In this study, we develop a particle trajectory simulation model for microsphere Y90 drug delivery, which provides an effective strategy to improve liver cancer therapeutics. The resin-based microspheres are chosen, and scanning electron microscopy is employed to provide accurate information of particle size used for the experimental validation. Results show the material properties of microsphere (density, size, friction constant), fluid properties (viscosity, flow velocity), and dimension of blood vessel (diameter, length, branch) are critical to the efficacy in delivery. The efficiency to the target can be effectively improved by adjusting the inertia–to-drag ratio (i.e., inversely proportional to Reynolds number). By throttling the GDA, the efficiency can be improved presumably due to the reduction of "dead zone" in the flow field. The work provides an effective approach to predict and improves the accuracy of Y90 microsphere-based drug delivery.



OC-2

Combination of Optimized Ligand Density and Magnetic Localization in Multifunctional Nanomedicine for Tumor therapy

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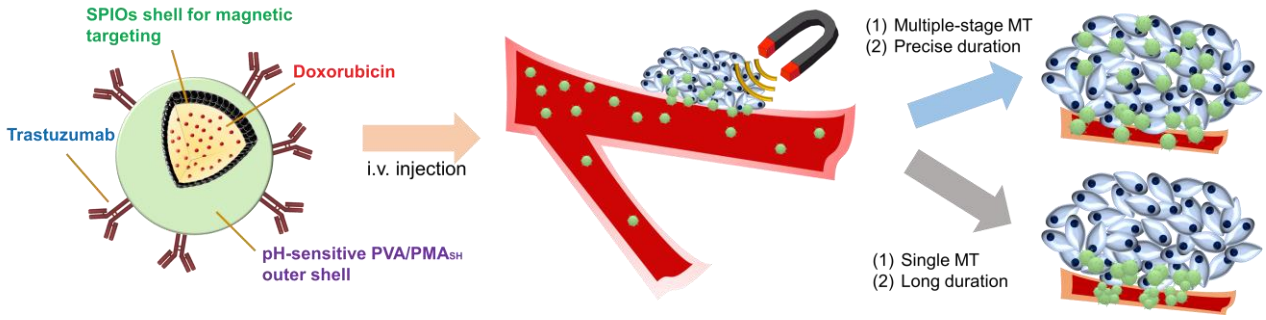
Although there has been encouraging progress in dual-targeting nanomedicines, the influence of cooperative interaction between magnetic targeting (MT) strategy and ligand density on a nanocarrier has been largely unexplored to date. In this study, we have synthesized a Trastuzmab (Tra)-immobilized, Doxorubicin (Dox)-encapsulated magnetic nanocapsules (T-Dox-MNCs) with dual targeting ability facilitated by modulating Tra density and MT approach. The MNCs comprising single component thiol-functionalized PVA/PMA_{SH} copolymer and superparamagnetic nanoparticles were developed for providing tunable dual-targeting functionality and simultaneously modulating pH-responsive on/off drug release. The 2T-Dox-MNCs with optimized Tra density bound to 87.3% of SKBR3 cells, and the effect was further promoted and bound to 95% of SKBR3 cells under MT application in 2 h incubation. Interestingly, Prussian blue stain of the tumor tissue demonstrated that a short-duration multi-stage MT (M-2h) can not only increase the accumulation of MNCs but improve intratumoral distribution. In contrast, MNCs were mostly aggregated in blood vessels in tumor under the single MT with long application duration (S-24h). Whereas MT appears to improve tumor accumulation, Tra-targeting results in greater retention following removal of the magnetic field. The mice treated with 2T-Dox-MNCs+M-2h showed 7.63-fold, 3.25-fold and 2.7-fold reduction in tumor volume compared to Dox-MNCs, 2T-Dox-MNCs and 2T-Dox-MNCs+S-12h. 2T-Dox-MNCs with precise ligand density and MT strategy represents a major paradigm advance in tumor treatment and design of dual targeted nanomedicine in clinical application.



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OC-3

Size-changeable Graphene Quantum Dot Nanotransformers for Penetrated Drug Delivery and Photothermal Therapy

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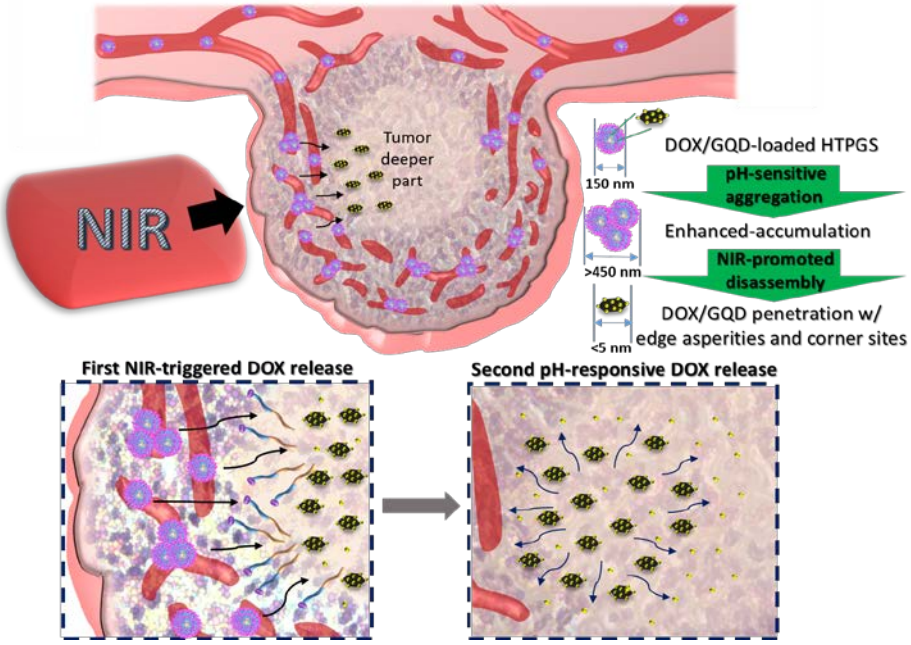
Delivery of therapeutic cargos within carriers that effectively accumulate at tumor promise to mitigate side effects and to improve the tumor therapeutic efficacy demanded for personalized medicine. Due to the tumor heterogeneity, however, these carriers which usually display low tumor accumulation and are piled up at the tumor's periphery near the blood vessels must address the issues in accumulation, penetration and transport sufficient cargos to the deep tumor for effective therapy. Here, a size-changeable graphene quantum dot (GQD) nanotheranostic that doubles as tumor accumulation agent with high cargo payload is developed to penetrate and sequentially release drug into deep tumor upon near-infrared irradiation. The nanotheranostic composed of ultrasmall GQD (5 nm) functionalized by amphiphlic pH-sensitive N-acetyl histidine-conjugated D-α-tocopherol polyethylene glycol 1000 succinate (HTPGS) that changes its size and aggregates at tumor through pH-sensitive surface exhibits a double increase in accumulation than the carriers without modification. Furthermore, this nanotheranostic can carry a large payload of anticancer drug, doxorubicin (DOX), on GQD and possess long half-life in circulation due to polyethylene glycol (PEG) of HTPGS. A size conversion of nanotheranostics at the tumor site was actuated by NIR irradiation which disassembles 150 nm of nanotheranostic into 5 nm of DOX/GQD, facilitating the penetration into the deep tumor tissue far from blood vessel, achieved by atomic-thin structure of GQD and hyperthermia. Followed by sequentially releasing DOX at low pH, GQD nanotheranostic integrates a penetrated photothermal-chemo therapy. Such size-changeable nanotheranostic integrated combination therapy successfully suppressed xenograft tumors in 18 days without distal harm when subjected to a single 15 min near infrared (NIR) laser treatment. This sophisticated GQD nanotheranostics with the capability of image tracking, enhanced tumor accumulation, NIR-triggered tumor penetration and hyperthermia ablation for photothermal-chemo therapy boosts tumor treatment and potentially uses in other biological applications.



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OC-4

Remotely Triggerable Microneedle as a Programmable Transdermal Delivery System for Analgesic Agents

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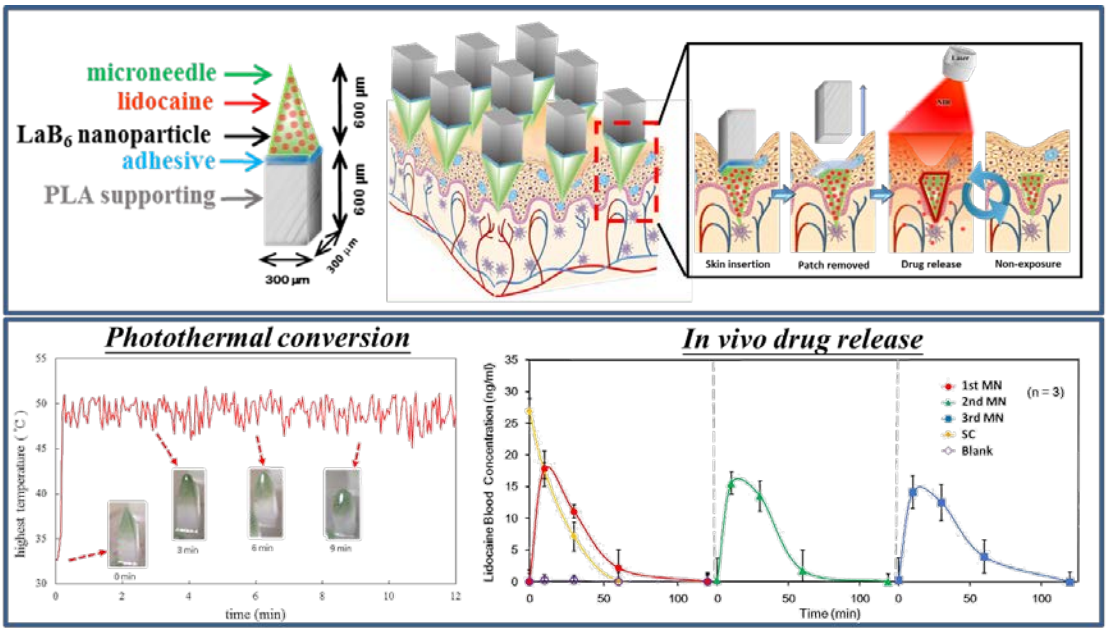
In this study, we used biodegradable polycaprolactone (PCL), encapsulated analgesic agent – lidocaine and lanthanum hexaboride (LaB_6) nanoparticles (NPs), to make remotely triggerable microneedle (MN). We focused on the feasibility of MN transdermally delivering analgesic agents and its safety assessment of clinical application. Lidocaine content in each MN patch was 1.58 ± 0.17 mg (n = 4). After giving treatment of NIR, LaB_6 NPs encapsulated in MN could convert the energy into heat leading to the melt of PCL and release drugs. The skin insertion tests showed that the microneedles could be fully inserted into the skin with penetration depth of 500~600 μm. The amount of released drugs can be controlled by adjusting the irradiation periods and exposure time and MN could be retriggered at least 6 cycles (3 min/cycle). Both skin scald observation and histological section confirmed that microneedles with 6 minutes NIR exposure performed the least heat damage to the skin tissue. The wound could recovered back to the original state after 12 hours. These result shows that there was no obvious heat damage in skin tissue after 6 minutes NIR exposure. We used inductively Coupled Plasma-Mass Spectroscopy (ICP-MS) to prove that LaB_6 NPs did not exist in the MN puncher site neither in other specific tissues after 24 hours from MN been applied. These results suggest that remotely controlled microneedles can be used safely under 6 minutes NIR exposure without any obvious damage to the skin tissue and preliminarily reassure its using safety.



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OC-5

Dependence of Delivery Performance and Antiglaucoma Efficacy of Antioxidant-Functionalized Intracameral Pilocarpine Carriers on Grafting Amount of Gallic Acid

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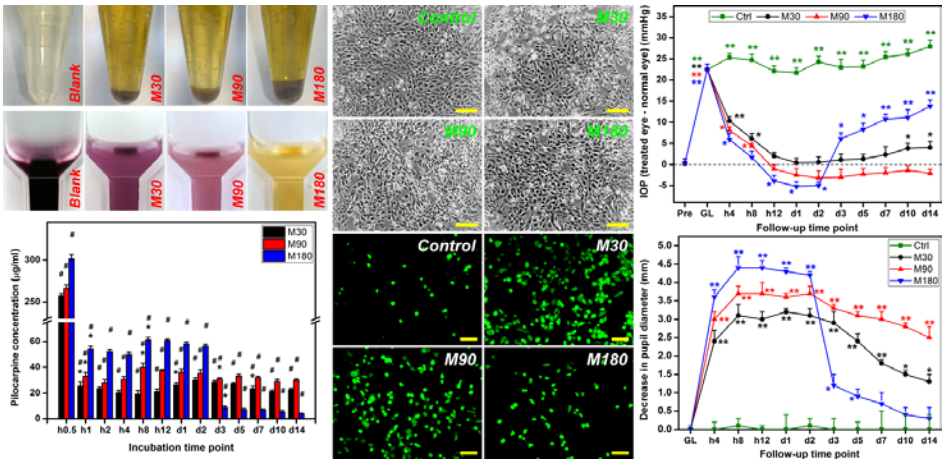
Functionalization of therapeutic carrier biomaterials can potentially provide additional benefits in drug delivery for disease treatment. Given that this modification determines final therapeutic efficacy of drug carriers, here, we investigate systematically the role of grafting amount of antioxidant gallic acid (GA) onto GN in situ gelling copolymers made of biodegradable gelatin and thermo-responsive poly(*N*-isopropylacrylamide) for intracameral delivery of pilocarpine in antiglaucoma treatment. As expected, increasing redox reaction time increased total antioxidant activities and free radical scavenging abilities of synthesized carrier biomaterials. The hydrophilic nature of antioxidant molecules strongly affected physicochemical properties of carrier materials with varying GA grafting amounts, thereby dictating in vitro release behaviors and mechanisms of pilocarpine. In vitro oxidative stress challenges revealed that biocompatible carriers with high GA content alleviated lens epithelial cell damage and reduced reactive oxygen species. Intraocular pressure and pupil diameter in glaucomatous rabbits showed correlations with GA-mediated release of pilocarpine. Additionally, enhanced pharmacological treatment effects prevented corneal endothelial cell loss during disease progression. Increasing GA content increased total antioxidant level and decreased nitrite level in the aqueous humor, suggesting a much improved antioxidant status in glaucomatous eyes. This work significantly highlights the dependence of physicochemical properties, drug release behaviors, and bioactivities on intrinsic antioxidant capacities of therapeutic carrier biomaterials for glaucoma treatment.



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OC-6

Core−Shell Structure, Biodegradation of Mixed Micelles of Atactic-PHB-mPEG and Isotactic-PHB-mPEG for Drug Delivery Systems

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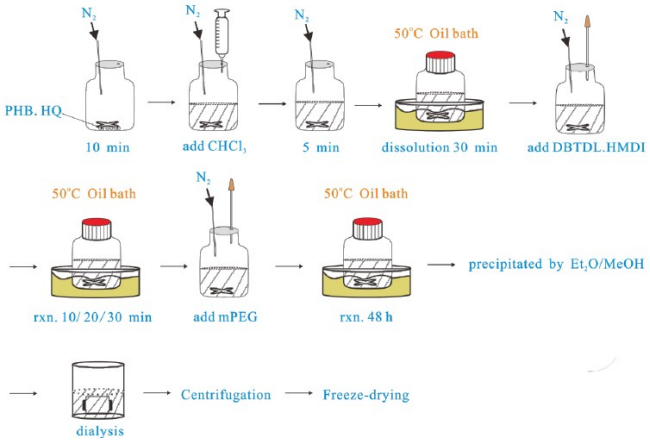
Amphiphilic block copolymers synthesized from biodegradable polymers have been explored in recent years. In an aqueous environment, they can self-assemble into polymeric micelles. Because of their unique features, such as small particle size, long-circulation time, and enhanced drug loading efficiency, micelles are widely used in drug delivery system.

In this study, we synthesized two types of diblock copolymers. For the first type, the diblock copolymer contains atactic poly[(*R*,*S*)-3-hydroxybutyrate] (a-PHB) and methoxy poly(ethylene glycol) (mPEG) as the hydrophobic and hydrophilic block, respectively. This copolymer was synthesized via ring opening polymerization of *β*-butyrolactone with mPEG as precursor. The second type diblock copolymer was synthesized from methoxy poly[(*R*)-3-hydroxybutyrate] (i-PHB) and mPEG with 1.6-hexamethylene diisocyanate (HMDI) as a coupling agent. These two types of copolymers showed significant difference in terms of their ability to form crystalline phase during micelle formation. The i-PHB-mPEG copolymer synthesized from nature PHB is semi-crystalline, while a-PHB-mPEG copolymer synthesized by the ring-opening polymerization is a totally amorphous. Therefore, the properties of the micelles can be tuned by mixing two types of copolymers in various ratios. The micelles with mixed copolymers were prepared by oil-in-water emulsion solvent evaporation method and the average diameter of the micelles was below 200 nm. From the observation of dynamic light scatting (DLS) and critical micelle concentration (CMC) experiments, it could be found that copolymers with the larger hydrophobic/hydrophilic ratio would form nanoparticles (NPs) in larger size and lower CMC, respectively. Further results such as drug loading capacity and efficiency will be presented in the poster. It is expected that the drug release behavior could be adjusted by mixing the drug-loaded micelles prepared from these two copolymers.



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OC-7

Photo-induced thermal-responsive nanogels for controlled drug release

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Environmentally-responsive nanogels have been widely used in controlled drug delivery in recent years. Many researches have been focused on the development stimulus-responsive nanogels.[1] Since temperature stimulus can be controlled more easily in comparison to other environmental stimuli, the development of thermo-sensitive nanogels has been the focus of many researches. In this study, we incorporated photosensitive molecules, sodium copper chlorophyllin (SCC),[2] into thermo-responsive nanogels made of copolymers of N-isopropylacrylamide (NIPAAm) and N-(hydroxymethyl)acrylamide (NHMAAm), and thus the nanogels could respond to a temperature (> 40℃) higher than the body temperature under the exposure to green laser light and then release anti-cancer drug, 5-FU (Figure 1).

We first investigated the thermal responsiveness of the nanogel in drug release (Figure 2). At 37℃, ~30% of 5-FU is released from nanogels within 9 h , while the amount of the 5-FU release reach ~67% within the same time interval at 50℃. On the other hand, when the drug-loaded nanogel was exposed to green laser for 2 min, a rapid burst of 5-FU was observed. Next, we examined the cell death by incubation of cells with the nanogel and green-laser exposure. The incubation of the cells with the 5-FU loaded nanogel alone did not cause significant cell death after 2 h (Figure 3). On the other hand, the cells that were incubated with the drug-free nanogel were killed significantly by green-laser exposure for 2 min. Further addition of the 5-FU loaded nanogel enhanced the cell-killing efficacy of the green-laser irridiation to ~60% mortality. Therefore, the elevated temperature and drug release exert an additive effect on cell killing. We expect that the nanogel could be applied potentially to cancer therapy.

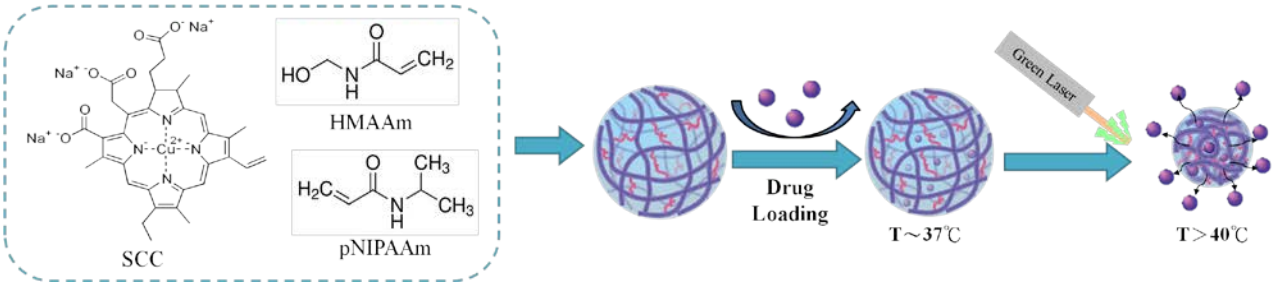

Figure.1 Experimental design

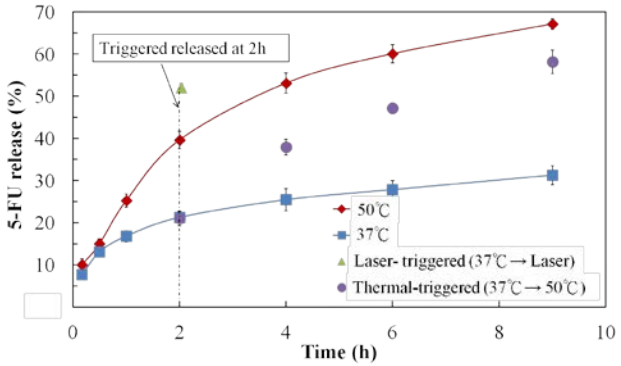

Figure.2 The release profile of 5-FU from the nanogels at 37 °C and 50 °C. The green triangle indicates the release of 5-FU after exposure to green laser for 2 min.

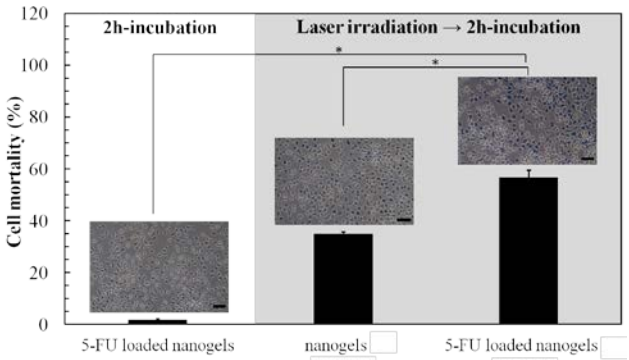

Figure.3 Green laser-induced cell-killing efficiency of 5-FU-loaded nanogels.

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OC-8

Development of Photosensitive Polymer/Gold Nanocomplexes for drug/gene delivery and Stem Cells-Based Therapy

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Inorganic nanoparticles have been widely applied for various biomedical applications. In this study, a novel type of polymer-gold nanocomplexes (SSPEI-Au NC) was designed and investigated for its potential on gene delivery. In parallel, polymer-gold nanorod (AuNR)-based materials were used to combine with tumor tropic adipose-derived stem cells (ADSCs) for their potential applications on stem cell-based photothermal and photodynamic therapy.

SSPEI-Au NC: The physicochemical properties of SSPEI-Au NC were characterized using UV-Vis spectroscopy, ZetaSizer and Transmission Electron Microscopy (TEM). *In vitro* transfection efficiency of SSPEI-Au NC was determined by fluorescence images and luciferase. The results indicate that SSPEI-Au NC/nucleic acid nanocomplex can effectively deliver nucleic acids into mammalian cells under serum-containing environment due to the effect of serum proteins-assisted colloidal stability on SSPEI-Au NC. It is worth mentioning that the transfection efficiency of SSPEI-Au NC was significantly higher than the commercial PEI25K under serum-containing environment. SSPEI-Au NC resulted in significantly lower cytotoxicity and higher transfection efficiency comparing to PEI25K (Fig 1).

Polymer-AuNR/ADSCs: The fabricated polymer-conjugated AuNR was successfully loaded with photosensitizer (Ce6) *via* electrostatic and hydrophobic interactions. The dispersion of polymer/AuNRI/Ce6 was explored using UV-Vis spectroscopy, ZetaSizer and TEM. The polymer/AuNRI/Ce6 nanocomplexes exhibited several favorable properties for drug delivery, including: well dispersion, high drug loading efficiency and GSH-sensitive drug release. In the *in vitro* co-culture setup, apoptosis of cancer cells were successfully induced by the surrounding polymer/AuNRI/Ce6 nanocomplexes-loaded ADSCs after light irradiation (Fig 2).

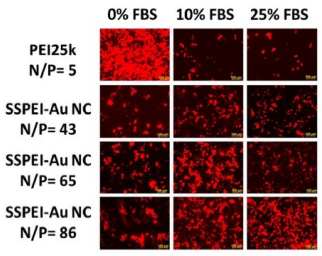

Figure 1. Effect of serum on the *in vitro* transfection.

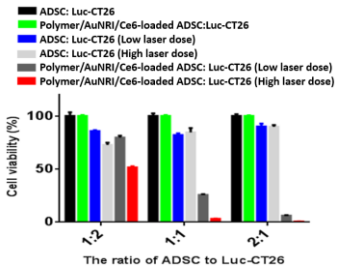

Figure 2. Study the killing effect after laser treatment.

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OC-9

Targeting effect of decorated SN38-loaded liposomes on MCF-7 cell line

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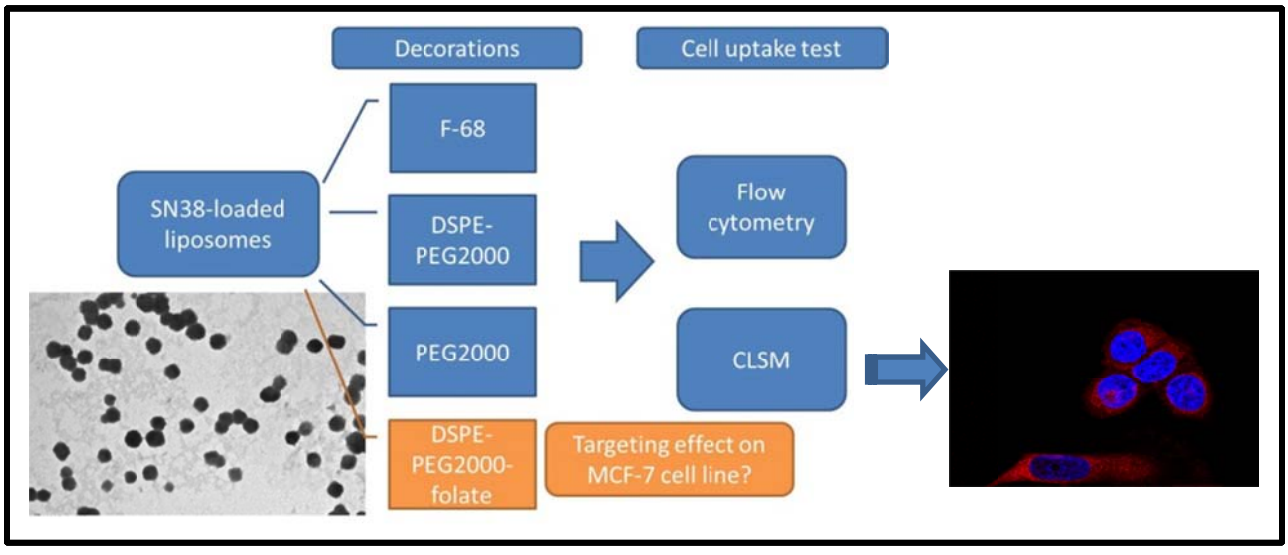
SN-38 (7-ethyl-10-hydroxycamptothecin) is an active and potent bio-metabolite of the commercial drug, irinotecan. However it possesses some drawback, for example the poor solubility, resulting in it unable to use. Therefore we would like to modified SN-38 through the pharmaceutical methods, that is, loading it into liposomes. We have designed a series of different decorated SN38-loaded liposomes. The decorations included Pluronic F-68 (poloxamer 188), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[amino (polyethylene glycol)-2000] (DSPE-PEG_{2000}) and polyethylene glycol-2000(PEG_{2000}).

We have discovered that with different decorations, the liposomes would have different physicochemical properties, includes particle size, polydispersity index (PDI), zeta-potential and encapsulating efficiency (EE%), but the release modes are the same. Our result showed that decorated SN38-loaded liposomes formulations had ideal particle size (69~104 nm), uniform particle size distribution (PDI < 0.2, except for the DSPE-PEG2000 groups) and well drug EE% (66~96%). In addition, the DSPE-PEG2000 groups had more negative zeta-potential (-45~-55 mV) compared to another groups (-3~-10 mV). In the release studies, all decorated liposomes followed Higuchi kinetics (R > 0.968) in 24 hrs.

Based on the primary results, we added another decoration, 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[folate(polyethylene glycol)-2000] (DSPE-PEG2000-folate), to investigate whether this decorated liposomes would have better targeting effect on the folate receptor overexpressing MCF-7 human breast adenocarcinoma cell line. We selected out two best formulations based on the cytotoxicity test. The two formulations were further conducted the flow cytometry test and confocal laser scanning microscopy(CLSM), to realize the *in vitro* cell uptake and selected a best formulation to carry on the next *in vivo* test.



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OC-10

A Novel Bupivacaine Emulsion for Postoperative Pain

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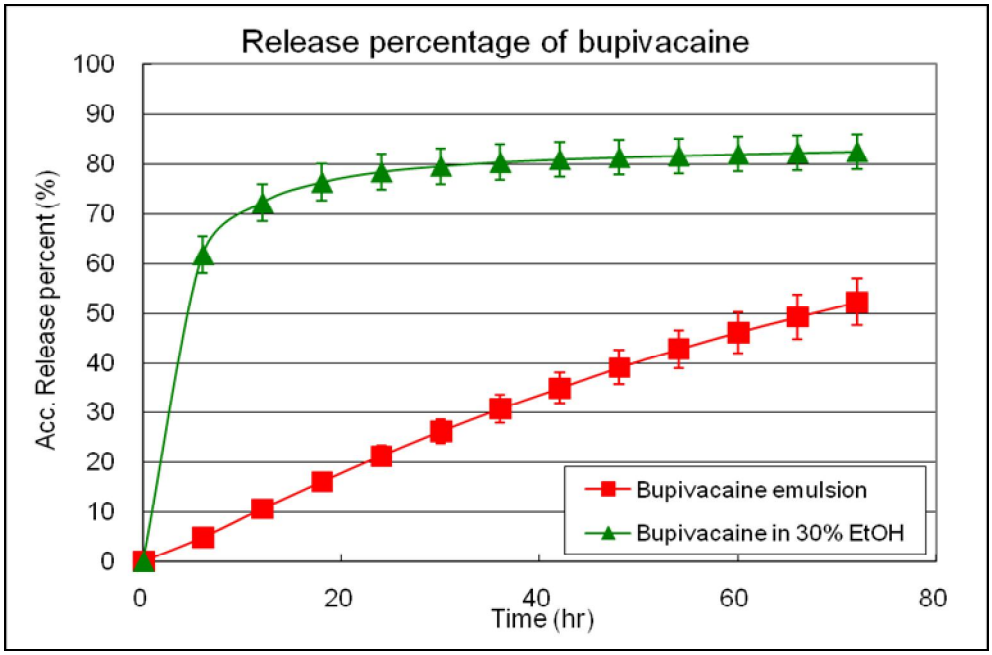
Local anesthetics play an important role in postoperative pain management. Bupivacaine is currently the longest acting local anesthetic approved by the FDA, with an analgesic effect lasting up to 18 to 24 hours[1]. However, bupivacaine has several well documented side effects, such as cardiovascular disorders and neurological disturbances. These side effects could be limited by applying it locally so as to reduce the administered doses and thus the concentration of bupivacaine in the blood. In this work, we have developed a novel emulsion formulation, to effectively maintain sustained local release of bupivacaine and thus reduce the drug concentration in systemic circulation. This newly developed emulsion formulation offers reduced toxicity and prolonged anesthetic effect for postoperative pain management.

Aside from the surfactant, we have selected a cyclic polysaccharide to be a key component at the interface between oil and aqueous phase[2]. The surfactant serves the function of reducing the interfacial tension of the emulsion[3] and modifying the release rate of bupivacaine. Various prototypes of this novel emulsion with the absence or presence of Tween 80 at different concentrations were prepared, and their droplet size and rate of bupivacaine release were determined. It was confirmed by Dynamic light scattering and optical microscopy images that the droplet size of the aforementioned emulsion system decreases with increasing concentration of Tween 80. Furthermore, approximately 52% of bupivacaine was released after 72 hours in nearly linear fashion. We believe that this novel emulsion formulation has potential in providing effective postoperative pain management.



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OC-11

Tumor-targeted nanoparticles co-deliver multi-inhibitors to overcome sorafenib-driven paradoxical activation of RAF/MEK/ERK pathway in hepatocellular carcinoma

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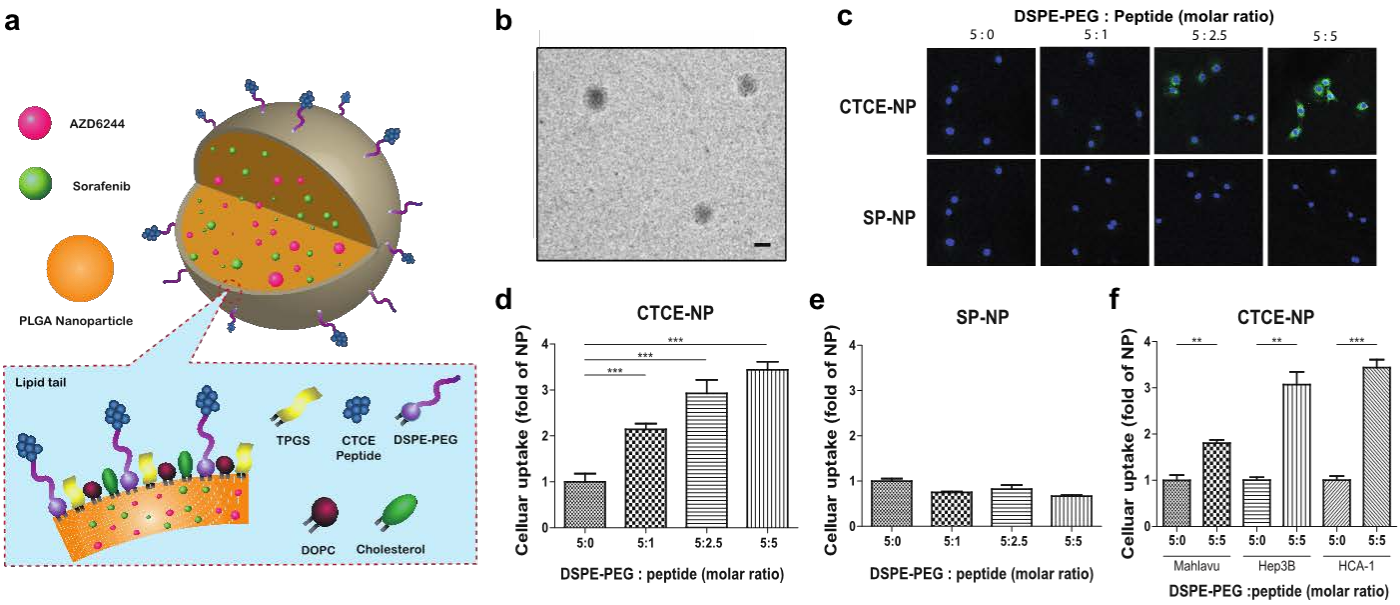
Inhibition of RAF with anti-cancer drugs may induce a "paradoxical" upregulation of the downstream mitogen-activated protein kinase (MAPK) pathway, i.e., the RAF/MEK/ERK signal transduction cascade, both in cancer and normal cells. Sorafenib is a RAF inhibitor approved for several cancers, including hepatocellular carcinoma (HCC). It is unknown whether "paradoxical" ERK activation occurs after sorafenib therapy in HCC, and has any role in treatment resistance. Here, we demonstrate that RAF inhibition by sorafenib rapidly leads to RAF dimerization and ERK activation in HCCs, which promotes treatment evasion. To overcome treatment evasion and reduce systemic effects, we developed HCC-targeted nanoparticles to co-deliver sorafenib with the MEK inhibitor AZD6244 in HCC. Using this approach, we selectively and efficiently downregulated RAF/ERK and PD-L1 expression, and facilitated intra-tumoral infiltration of cytotoxic CD8+ T cells. These effects resulted in a profound delay in tumor growth. Thus, this nano-delivery strategy to selectively target tumors and prevent the paradoxical ERK activation could increase the feasibility of dual RAF/MEK inhibition to overcome sorafenib treatment escape in HCC.



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OC-12

Biodegradable Polymer/SPIO Nanocomplexes for Efficient Magnetofection, Magnetic Resonance Imaging and Anti-Cancer Therapy

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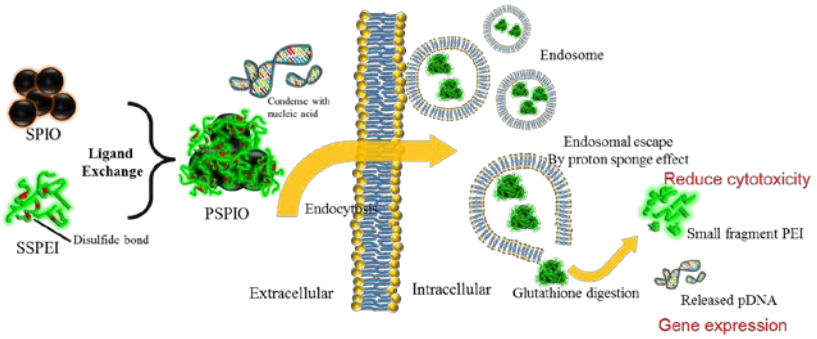
In recent year, the combination of cationic polymers with superparamagnetic iron oxide nanoparticles (SPIO) has attracted significant attention for its great potential on magnetic resonance imaging (MRI) and gene delivery. For example, nondegradable branched polyethylenimine (bPEI 25kDa) has been modified onto the magnetic nanoparticle (MNP) for efficient gene delivery; however, the cytotoxicity of nondegradable bPEI has limited its further *in vivo* applications. To tackle with this issue, we proposed a novel nanocomplex system (PSPIO) consisting of bioreducible PEI and SPIO for gene delivery and MRI applications. The physicochemical properties of PSPIO were characterized in details. PSPIO exhibited proper particle size (115 nm), great protection of nucleic acids from DNase, well-dispersive colloids in presence of serum, and redox-responsive pDNA release. The aforementioned properties suggest PSPIO could be used as a potential gene carrier. In addition, PSPIO provided significant T2 imaging contrast enhancement (r2= 291.1 s^{-1} ·mM^{-1}) measured using a 7T MRI system. Comparing to nondegradable bPEI 25kDa, PSPIO dsiplayed negligible cytotoxicity and higher transfection efficiency under *in vitro* biomimicking conditions. In a parallel study, we developed another magnetofection system (PNT) specifically for human mesenchymal stem cells (hMSCs). PNT was able to deliver an antineoplastic pDNA containing TNF-related apoptosis-inducing ligand (TRAIL) cDNA, into hMSCs ($^{PNT/TRAIL}$hMSCs) with very high expression level. Moreover, PNT-mediated magnetofection did not reduce the tumor tropism of hMSCs. The preliminary *in vivo* study showed that $^{PNT/TRAIL}$hMSCs were able to inhibit tumor growth on an orthotopic human glioma-bearing mouse model.



Scheme. PSPIO-Mediated Gene Delivery into Mammalian Cells

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OC-13

Porous Lipids@Silica/Carbon Nanosheets with Magnetic Stimulation in Enhanced Neural-like Cell Differentiation and Cancer Therapy

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Non-invasive treatment has been increasingly advocated and relatively safe. Therefore, we merged the concept of non-invasive therapy and chemotherapy to produce a carrier having conductivity, nanoscale and biocompatible. To meet the above ideas, we adopt graphene oxide as a template and coating silica on the surface. The product is a porous silica/carbon (PSC) nanosheets. In order to increase biocompatibility, we modified the mixed lipids (DOPC+ DPPC) on the PSC surface. Finally, we can make the porous lipids@ silica/carbon nanosheets (PLSC) to encapsulate drugs.

Then, we apply Oersted's law and Lenz's law as a mechanism to non-invasive treatment. Put the PLSC into High Frequency Induction Heating Machine and take advantage of conductive properties, we can get the induced current in the carrier.

Finally, we applied to the non-invasive treatment of nerve repair and tumor suppressor. Such treatments is safer and cheaper.

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OC-14

Multifunctional GCSF-Containing Nanoparticles for Oral Delivery to Chemotherapy-Induced Neutropenia Rat

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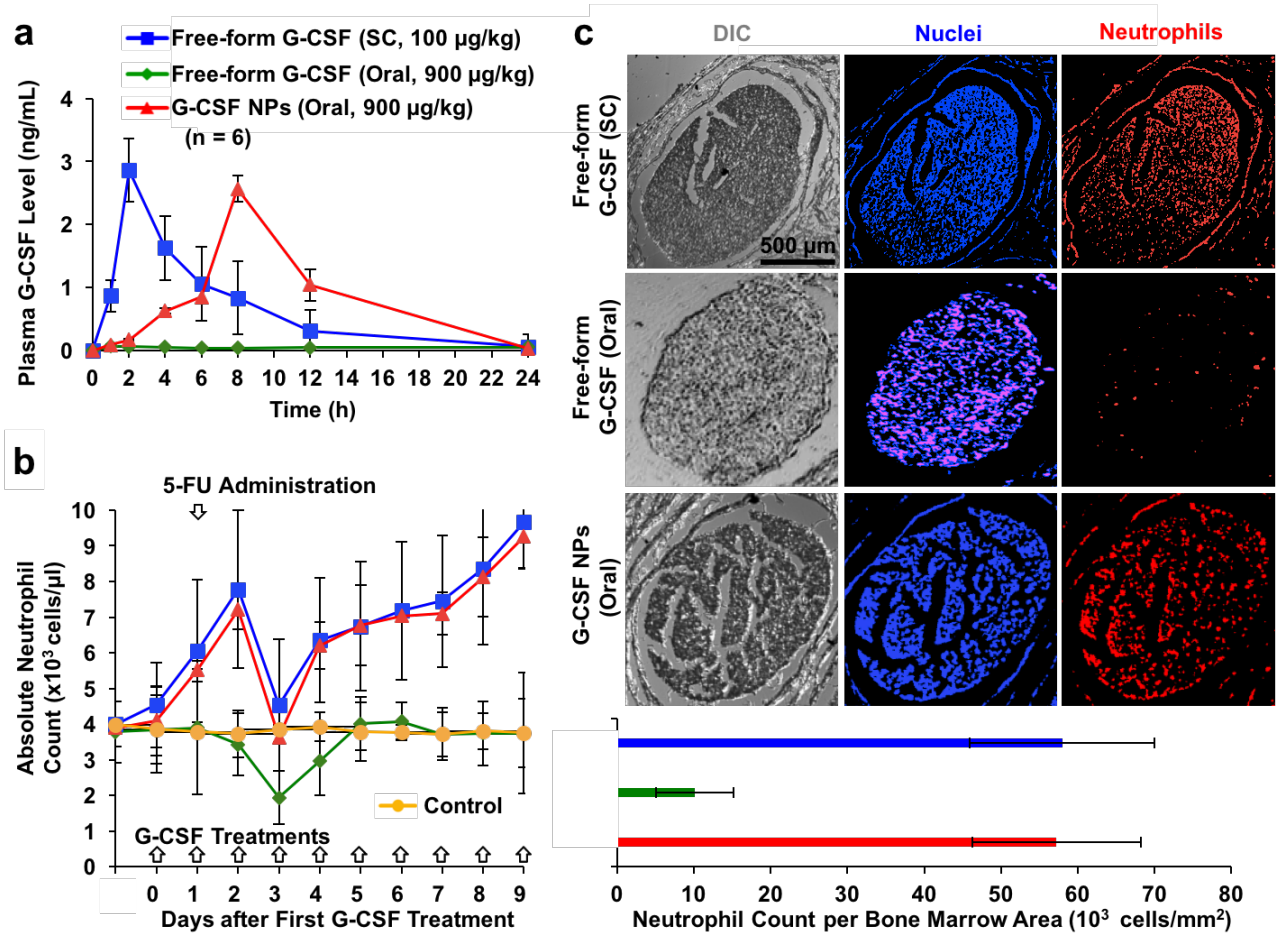
Chemotherapy-induced neutropenia often increases the likelihood of life-threatening infections. In this study, a nanoparticl(NP) system composed of chitosan and poly(γ-glutamic acid) conjugated with diethylene triamine pentaacetic acid (γPGA-DTPA) was prepared for oral delivery of granulocyte colony-stimulating factor (G-CSF), a hematopoietic growth factor. The therapeutic potential of this NP system for daily administration of G-CSF to treat neutropenia associated with chemotherapy was evaluated in a rat model. *In vitro* results indicate that the procedures of NP loading and release preserved the structural integrity and bioactivity of the G-CSF molecules adequately. Those results further demonstrated the enzymatic inhibition activity of γPGA-DTPA towards G-CSF against intestinal proteases. Additionally, the *in vivo* biodistribution study clearly identified accumulations of G-CSF in the heart, liver, bone marrow, and urinary bladder, an indication of systemic absorption of G-CSF; its relative bioavailability was approximately 13.6%. Moreover, significant glucose uptake was observed in bone marrow during G-CSF treatment, suggesting increased bone marrow metabolism and neutrophil production. Consequently, neutrophil count in the blood increased in a sustained manner; this fact may help a patient's immune system recover from the side effects of chemotherapy.



壁報論文競賽

PB-1

Human Hair Keratin as a Template for Cell Adhesion and Adipose-derived Stem Cell Differentiation

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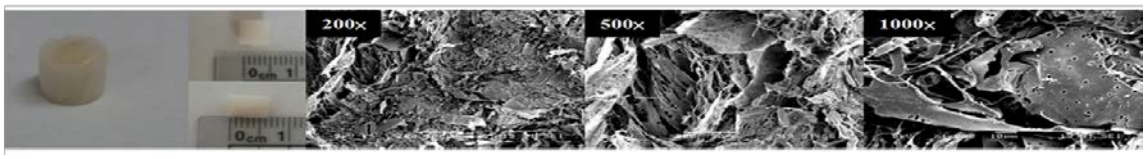
Keratin biomaterials derived from human hair have raised researcher's interests due to the intrinsic ability to interact with different types of cells and the potential to serve as a controllable extracellular matrix protein which can be used in studies of cell mechanism, *in vitro*/*in vivo* response, and cell-matrix interaction. However, the interaction between keratin and stem cells has not been well reported. In the present study, we investigate the effect of keratin biomaterials to the growth of porcine adipose stem cells (pASCs) as well as a series of selective cell lines. pASCs on keratin coating demonstrated enhanced adhesion, proliferation and differentiation. Evaluation of genetic markers showed that adipogenic and osteogenic differentiation can be successfully induced without abnormal morphologies. *in vitro* and *in vivo* studies of coatings and scaffolds also support keratin's potential for biomedical application. Therefore, the combination of keratin biomaterials with stem cells may provide additional benefits in various bioengineering approaches.



Actual appearance and SEM images of human hair keratin.

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PB-2

Fixation of Fibronection on Aligned Electrospun Polyhydroxyalkanoate Scaffold Using Surface Modification Method for Vascular Tissue Engineering

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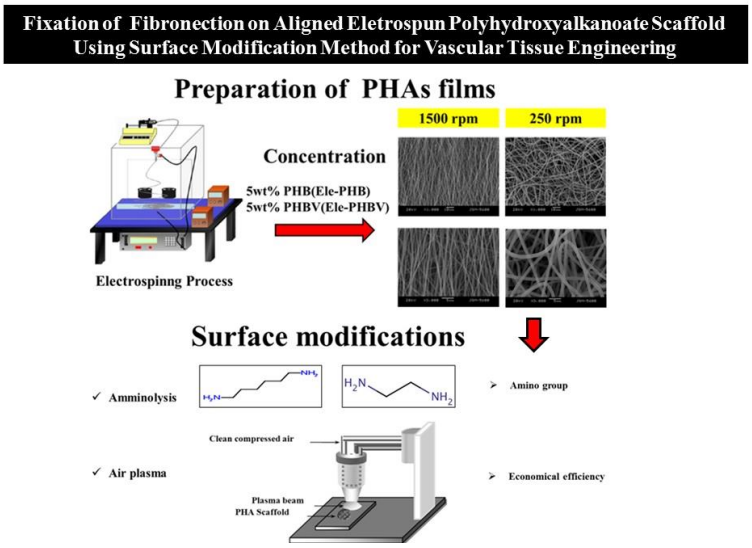
Repair and regeneration of vascular tissue is an important research topic of current biomedical engineering and regenerative medicine. Many studies indicated that cells need to grow on the suitable extracellular matrix to show the particular functionality. In our study, we tested various surface modifications to fix the ECM (fibronectin and collagen were selected) on the biodegradable polymer surface (poly(3-hydroxybutyrate, PHB and poly(3-hydroxybutyrate-co-3-hydroxyvalerate), PHBV). In this study, alignment PHB and PHBV films were prepared using electrospinning method. The surface modification of alignment PHB and PHBV were using amminolysis or air plasma treatment, and then were treated with EDC/NHS solution to further fix with ECM. In addition, the cytotoxicity and biocompatibility of surface modified films were checked by 3T3 and L929 cell line culture. The endothelial cell viability and proliferation were checked by EPC and HUVEC (as control) culture.

The results showed that the surface of alignment PHB and PHBV films can be modified successfully by chemical methods based on ninhydrin assay and contact angle assay. XPS assay also confirmed ECM has immobilized on the film. In addition, the WST-1 assay, immunocytochemistry assay and SEM showed that the surface modified films performed excellent cell compatibility. Taken together, our results demonstrated that PHB and PHBV films that were modified by the above chemical method and were fixed with suitable ECM can provide a potential artificial vessel for application of vascular tissue engineering.



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PB-3

Silver-Silica Hybrid Nanoparticles for Biomedical Applications

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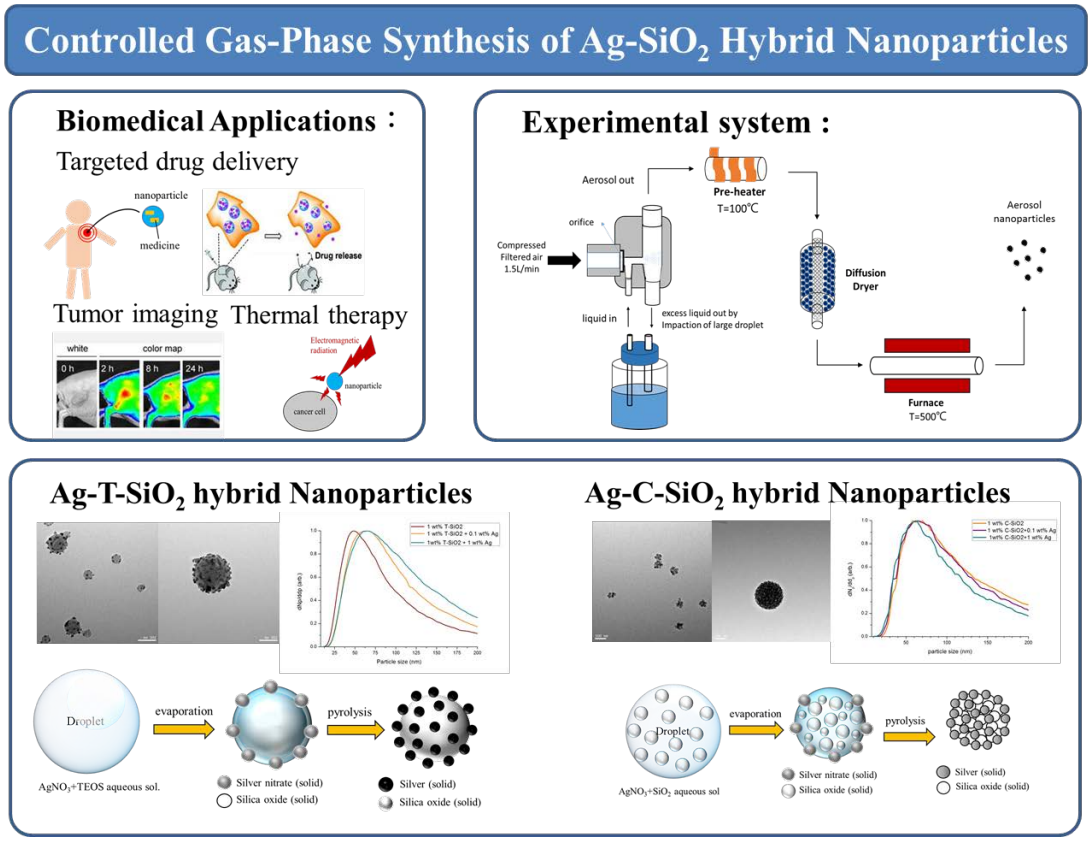
In this work we develop a new strategy to synthesize silver-silica hybrid nanoparticles (Ag-SiO_2 NP) using an aerosol-based approach. The method includes the use of a downstream particle size classification for characterization and also size purification, by which we obtain Ag-SiO_2 NPs with high purity in elemental compositions and provide the capability to control the monodispersity in the primary diameter. Differential mobility analysis, transmission electron microscopy, thermogravimetric analysis, and x-ray diffractometry were employed orthogonally to provide the information of heating temperature and concentrations of precursors versus material properties. Results show silver nanoparticles (AgNPs) were able to decorate on spherical, size-controlled silica nanoparticles to form the hybrid nanostructure using tetraethoxysilane as SiO_2 precursor. By using silica colloids with different concentration as precursor, AgNPs nucleated and grew at the interstitials of spherical SiO_2 nanoparticle clusters to form the hybrid structure. The size of AgNP in the hybrid nanostructure were shown to be proportional to the concentration of Ag precursor, and the size of SiO2 cores was dependent of the selected mobility size and the concentration of SiO_2 precursor. The surface plasmonic resonance (SPR), colloidal stability, and dispersibility of AgNPs in an aqueous environment enhanced significantly after hybridization with SiO_2. Our work provides a generic way to implement the design of fabricating AgNP-SiO_2 NP through a well-controlled synthesis route for emerging biomedical applications (e.g., hyperthermal therapy, targeted drug delivery).



PB-4

Kinetic Study of Ligand-Silver Nanoparticle Interactions to Colloidal Stability

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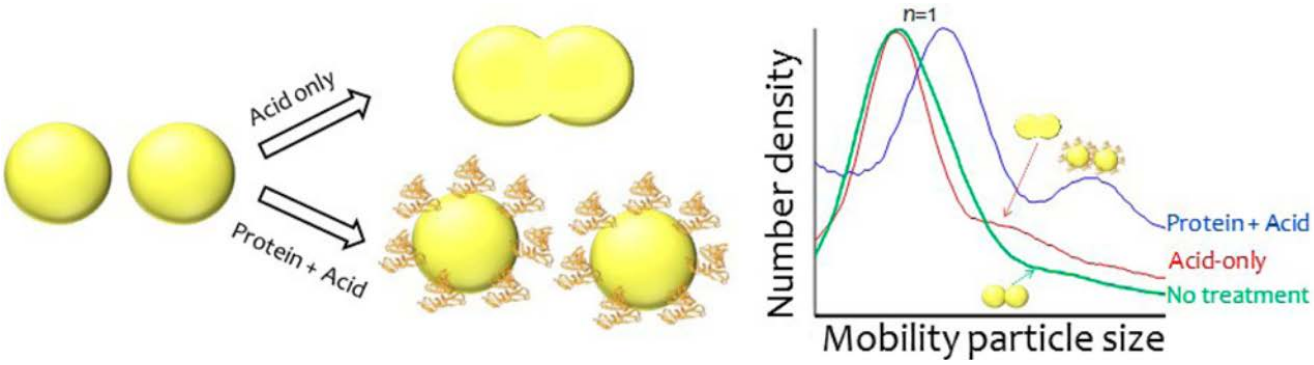
We report a kinetic study of Ag nanoparticles (AgNPs) under acidic environments and systematically investigate the impact of ligand interactions [i.e., bovine serum albumin (BSA) and thiol-Polyethylene glycol (SH-PEG) as representatives] to the colloidal stability of AgNPs. Electrospray-differential mobility analysis (ES-DMA) was used to characterize the particle size distributions and the number concentrations of AgNPs. Transmission electron microscopy was employed orthogonally to provide visualization of AgNPs. For unconjugated AgNPs, the extent of aggregation, or the average particle size, was shown to be increased significantly with an increase of acidity, where a partial coalescence was found between the primary particles of unconjugated AgNP clusters. We observe BSA and SH-PEG had a strong binding affinity (equilibrium binding constant, > 105 L/mol) to the surface of AgNPs. BSA-functionalized AgNPs exhibited highly-improved colloidal stability compared to the unconjugated AgNPs under acidic environments, where both the acid-induced interfacial dissolution and the particle aggregation became negligible. In contrast, SH-PEG-functionalized AgNPs dissolved gradually in an acidic environment. Results confirm a complex mechanism of colloidal stability of AgNPs: the aggregation process was shown to be dominant, and the formation of BSA corona on AgNPs suppressed both particle aggregation and interfacial dissolution of AgNP samples under acidic environments. The presence of SH-PEG provided the steric hindrance against aggregation but not for surface dissolution. The work presented here provides a proof of concept for the investigation of colloidal stability of AgNPs over various formulation chemistry and environment conditions (e.g., cell culture media and natural water). This prototype methodology we demonstrate here can be applied to other types of NP-based platforms (e.g., metal oxides NPs) combining surface interactions with proteins and other molecular species.

Key words: silver, BSA, SH-PEG, Electrospray-Differential Mobility



FQuote fromor Langmuir, 2014, 30 (43), pp 12755–12764

PB-5

Assembly of Functional Gold Nanoparticle on Silica Microsphere

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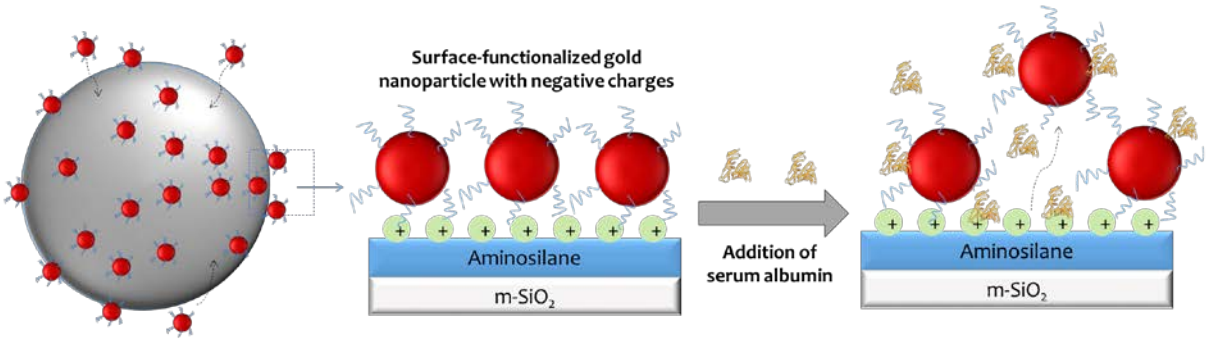
We demonstrate a controlled synthesis of silica microsphere with the surface-decorated functional gold nanoparticles. Surface of silica microsphere was modified by 3-aminopropypltriethoxysilane and 3-aminopropyldimethylethoxysilane to generate a positive electric field, by which the gold nanoparticles with the negative charges (unconjugated, thiolated polyethylene glycol functionalized with the traceable packing density and conformation) were able to be attracted to the silica microsphere. Results show that both the molecular conjugation on gold nanoparticle and the uniformity in the amino-silanization of silica microsphere influenced the loading and the homogeneity of gold nanoparticles on silica microsphere. The 3-aminopropyldimethylethoxysilane-functionalized silica microsphere provided an uniform field to attract gold nanoparticles. Increasing the ethanol content in aminosilane solution significantly improved the homogeneity and the loading of gold nanoparticles on the surface of silica microsphere. For the gold nanoparticle, increasing the molecular mass of polyethylene glycol yielded a greater homogeneity but a lower loading on silica microsphere. Bovine serum albumin induced the desorption of gold nanoparticles from silica microsphere, where the extent of desorption was suppressed by the presence of high-molecular mass polyethylene glycol on gold nanoparticles. This work provides the fundamental understanding for the synthesis of gold nanoparticle-silica microsphere constructs useful to the applications in chemo-radioactive therapeutics.

KEYWORDS. Gold, nanoparticle, silica, microsphere, polyethylene glycol, aminosilane, deposition, serum albumin, stability



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PB-6

Gellan gum/Glucosamine films carrying 5-Chloro-8-hydroxy-7-iodoquinoline as an oral cancer treatment patch

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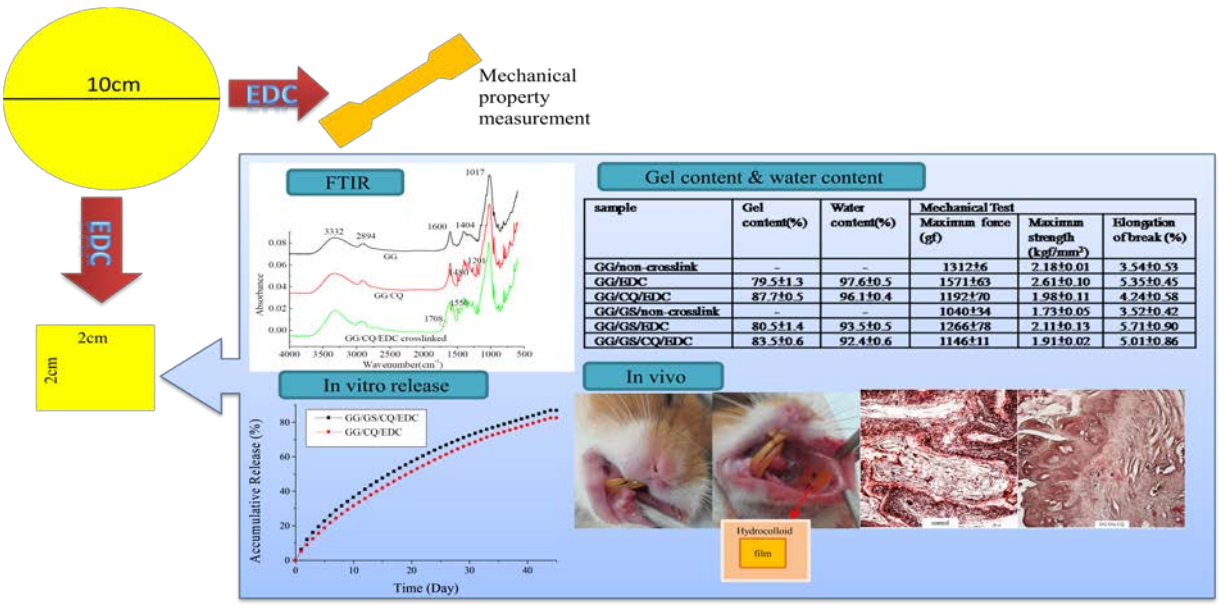
Every year, worldwide nearly 1/2 million patients will be diagnosed with oral cancer and approximately 150,000 patients die each year. Treatment for oral cancer is dependent on the stage of development of the cancer. The study aims to design gellan gum-based oral cancer treatment patch, which include chemotherapy drugs (5-Chloro-8-hydroxy-7-iodoquinoline, CQ) not only can be used in early stages of oral cancer treatment but also can be used the wound care dressing after surgery in late-stage of oral cancer treatment. The results showed that the CQ can via the EDC-mediated covalent conjugation with gellan gum (GG/CQ) and gellan gum/glucosamine (GG/GS/CQ).The gel content of GG/CQ and GG/GS/CQ films were 87.7±0.5 and 83.5±0.6, respectively. The water content of GG/CQ and GG/GS/CQ films were 96.1±0.4 and 92.4±0.6, respectively. Mechanical testing revealed that the maximum tensile strength and elongation at break of the GG/CQ film were 2.61 kgf/mm2 (25.59 Mpa) and 5.35%, respectively. Mechanical testing revealed that the maximum tensile strength and elongation at break of the GG/GS/CQ film were1.91 kgf/mm2 and 5.01%.Drug release experiment had lasted 45 day, the amount of CQ released from GG and GG/GS membranes were 82.4% and 86.8%.Huguchi model fits the GG/CQ and GG/GS/CQ release data with high correlation coefficients (R^2=0.9990 and 0.9994).This study confirmed that CQ release from GG or GG/GS membrane with constant rate of diffusion, without burst effect and these system suitable be design to achieve prolonged therapeutic action in vivo. To evaluate the cytotoxic effect of CQ, human oral cancer cell line OC-2 was treated with DMSO or various concentrations of CQ for 24 h. From the date, we founded that the amount of CQ release from GG or GG/GS membrane reach doses high enough to kill oral cancer cells with or without $CuCl_2$.Finally, we set up animal models for oral cancer research and investigated effectiveness and clinical application of gellan gum-based membrane as oral cancer treatment patch.



sample	Gel content(%)	Water content(%)	Mechanical Test		
			Maximum force (gf)	Maximum strength (kgf/mm²)	Elongation of break (%)
GG/non-crosslink	-	-	1312±6	2.18±0.01	3.54±0.53
GG/EDC	79.5±1.3	97.6±0.5	1571±63	2.61±0.10	5.35±0.45
GG/CQ/EDC	87.7±0.5	96.1±0.4	1192±70	1.98±0.11	4.24±0.58
GG/GS/non-crosslink	-	-	1040±34	1.73±0.05	3.52±0.42
GG/GS/EDC	80.5±1.4	93.5±0.5	1266±78	2.11±0.13	5.71±0.90
GG/GS/CQ/EDC	83.5±0.6	92.4±0.6	1146±11	1.91±0.02	5.01±0.86

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PB-7

Understanding Ligand–Nanoparticle Interactions for Silica, Ceria, and Titania Nanopowders

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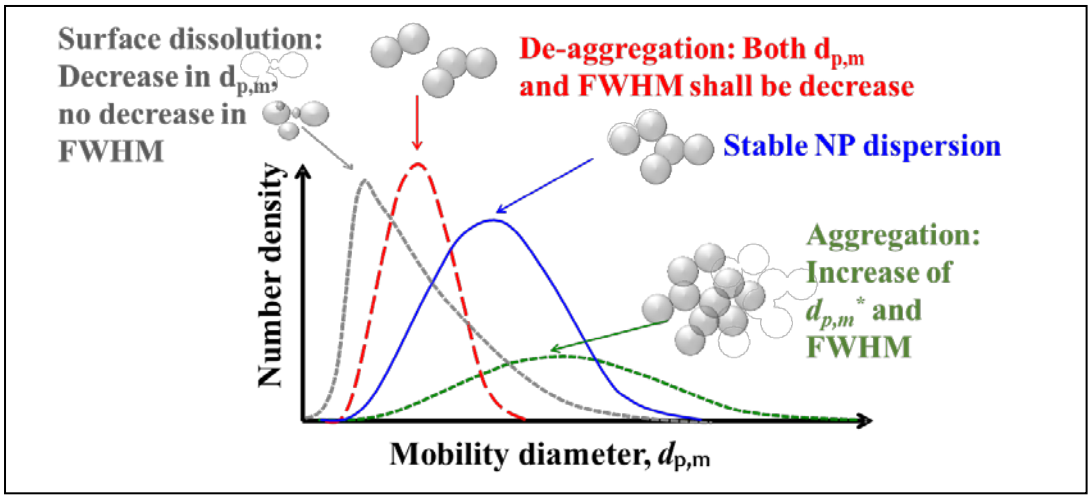
We perform a study on aqueous suspensions of three types of nanoparticles (TiO2-NPs, CeO2-NPs,SiO2-NPs) and investigate the material properties and the surface reaction with surfactant-type ligands to their subsequent colloidal stability, the key factors to their impact on the environmental health and safety (EHS). Bovine serum albumin, sodium dodecyl sulfate, and cetyltrimethylammonium bromide were used as representative surfactant ligands. Electrospray differential mobility analysis, dynamic light scattering, zeta potential measurement, transmission electron microscopy, inductively coupled plasma mass spectrometry, x-ray diffraction spectrometry were employed orthogonally to obtain particle size, morphology, surface corona, concentration and composition, and the change in colloidal stability. Results show that colloidal stability was strongly affected by the surface properties of nanoparticles and the subsequent interactions with ligands under different environmental conditions. Aggregation was shown to be the dominant process to colloidal instability. Our work demonstrates a prototype study to investigate the change of surface charges and the fate of nanomaterial's colloidal stability after interacting with ligands and their subsequent impact in EHS.



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PB-8

Producing 3D hBMSC Spheroids SF/PCL Hybrid Cardiac Patches by Regulating Mechanical Property of the Substrates

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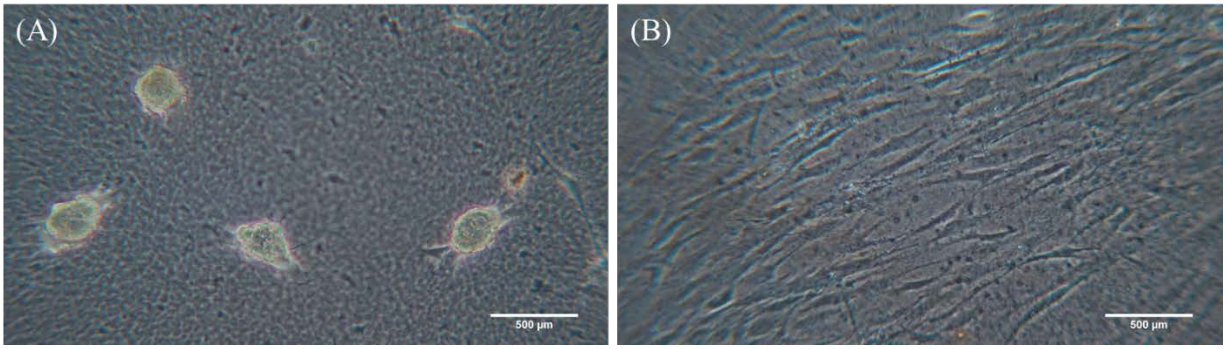
Recently, 3-dimentional cell culture has been intensively investigated due to high similarity between cell spheroid and normal tissue. Benefits of cytokine secretion and better differentiation of cell spheroids compared with 2D monolayers have also been documented. In this study, cardiac patches composed by poly (ε-caprolactone) (P) grafted with SF of various β-sheet content (crystallinity, %) were fabricated to regulate mechanical properties of substrates for investigating the effects of crystallinity on the cardiomyogenesis of hBMSC after induced by 5-aza. Various crystallinities were examined by ATR-FTIR and analyzed by Fourier-deconvolution method. Young's modulus, AFM and SEM were used to characterize mechanical property and surface topography of the patches. The crystallinities of various cardiac patches were 20%, 30%, 37% and 44%, abbreviated as PSC20, PSC30, PSC37 and PSC44, respectively. The values of Young's modulus of PSC patches were increased with the increasing crystallinity values. In addition, nano-scale particles were observed by the images of SEM and AFM especially in PSC44 patches which could be due to ethanol treatments. After three-day cultivation, live/dead stain revealed good proliferation of hBMSC on various patches. Besides, spheroid formations of hBMSC onto PSC20 and PSC30 patches while forming 2D monolayer of the cells onto PSC44 patches were observed. Notably, hBMSC spheroids showed significantly higher expressions in cardiac specific proteins such as Connexin 43 than those of hBMSC monolayers ($p<0.05$, $n=3$). In conclusion, 3D hBMSC spheroids PSC hybrid cardiac patches with promoting cardiomyogenesis of hBMSC can be produced by regulating mechanical properties of PSC substrates via varying crystallinity.

(A) hBMSC spheroid on PSC20 cardiac patch, and (B) hBMSC monolayer on PSC44 cardiac patch.



PB-9

Electrospun PEG-NPs/PHB Nanocomposite Fibrous Membranes As Potential Biomaterial For Tissue Engineering

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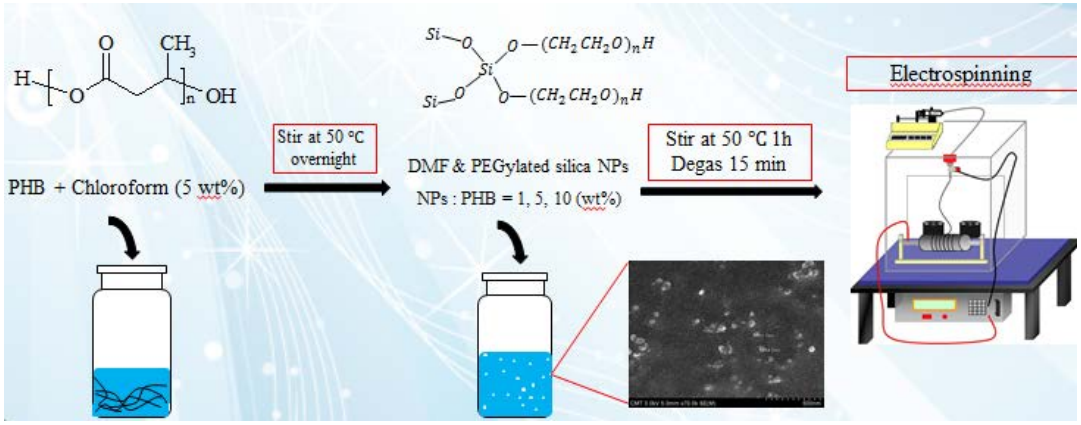
Poly(R-3-hydroxybutyrate) (PHB) is a biocompatible and biodegradable polymer, and it has been considered as a potential material for tissue engineering. Tensile strength of PHB is quite strong and comparable to commercial polypropylene, but its brittleness have been the main disadvantages in potential applications. In order to remedy the weakness, incorporation of PEGylated silica nanoparticles (PEG-NPs) into PHB is attempted. In this study, the mechanical properties of the electrospun PEG-NPs/PHB nanocomposite fibrous membranes are evaluated. The performance of the membranes in cell culture of 3T3 fibroblasts and tenocytes is investigated for possible applications in tendon healing. Mono-dispersed PEGylated silica NPs were first prepared by grafting methoxypolyethlene glycol 2000 on the surface of silica NPs during the sol-gel synthesis process. The electrospun nanocomposite PHB fibrous membranes were prepared with various contents of PEG-NPs. The SEM images showed that fibrous membranes of the PEG-NPs/PHB nanocomposite could be successfully prepared. The mechanical properties of the membranes and the preliminary cell culture results will be presented.



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PB-10

Investigation of Overrun-Processed Porous Hyaluronic Acid Carriers in Corneal Endothelial Tissue Engineering

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Hyaluronic acid (HA) is a linear polysaccharide naturally found in the eye and therefore is one of the most promising biomaterials for corneal endothelial regenerative medicine. This study reports, for the first time, the development of overrun-processed porous HA hydrogels for corneal endothelial cell (CEC) sheet transplantation and tissue engineering applications. The hydrogel carriers were characterized to examine their structures and functions. Evaluations of carbodiimide cross-linked air-dried and freeze-dried HA samples were conducted simultaneously for comparison. The results indicated that during the fabrication of freeze-dried HA discs, a technique of introducing gas bubbles in the aqueous biopolymer solutions can be used to enlarge pore structure and prevent dense surface skin formation. Among all the groups studied, the overrun-processed porous HA carriers show the greatest biological stability, the highest freezable water content and glucose permeability, and the minimized adverse effects on ionic pump function of rabbit CECs. After transfer and attachment of bioengineered CEC sheets to the overrun-processed HA hydrogel carriers, the therapeutic efficacy of cell/ biopolymer constructs was tested using a rabbit model with corneal endothelial dysfunction. Clinical observations including slit-lamp biomicroscopy, specular microscopy, and corneal thickness measurements showed that the construct implants can regenerate corneal endothelium and restore corneal transparency at 4 weeks postoperatively. Our findings suggest that cell sheet transplantation using overrun-processed porous HA hydrogels offers a new way to reconstruct the posterior corneal surface and improve endothelial tissue function.

PB-11

Development of Gelatin-Functionalized Silver Nanoparticles for Corneal Stromal Tissue Engineering

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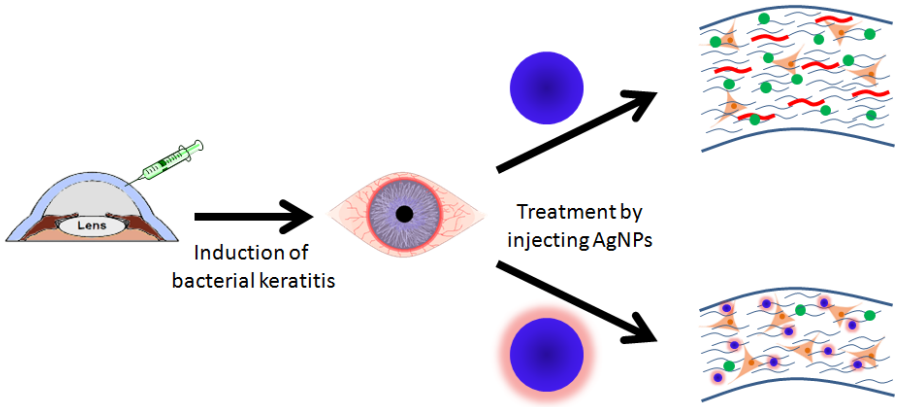
Bacterial keratitis is a common and severe ocular infection and one of the key causes of blindness and corneal dysfunction throughout the world. It can cause damage to the corneal layer thereby affecting vision. The use of antibiotic eye drops is common for those who have an eye infection. Moreover, bacterial keratitis may accompanied by corneal neovascularization. Therefore, in order to overcome these disadvantages, we develop the gelatin-capped silver nanoparticles with antibacterial and antiangiogenic properties. The drawbacks of silver nanoparticles can be improved by modified biopolymer. The obtained results suggested that gelatin-functionalized silver nanoparticles improve the effect as biocompatibility, antibacterial activity, antiangiogenic ability, residence time, and ameliorate validly symptoms of bacterial keratitis compare with non-gelatin capping group. Upon these findings, we proposed that gelatin functionalized silver nanoparticles may be considered as improved ocular delivery system for the treatment of bacterial keratitis.



PB-12

Iron Oxide/Graphene Oxide Nanocomposites for Magnetically and Photothermally Enhanced Gene Delivery into Suspension Cells

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Abstract

The low transfection efficiency of non-viral vectors is the main problem and that is difficult to carry genes into cells, not to mentioning multiple genes or large plasmids (i.e., CRISPR/Cas9 or Episomal plasmids) into cells. Although many non-viral vectors, including liposome, calcium phosphate, have been successfully developed for transfection of various adherent cell lines, some types of cells such as primary cells and suspension cells are still hard to transfect. Therefore, the development of efficient non-viral carriers to solve those difficulties in transferring cells becomes imortant. In this work, we developed a multifunctional non-viral vector integrated nanoscale graphene oxide (nGO) and superparamagnetic iron oxide nanoparticles (Fe_3O_4) for carrying genes into suspension cells. The nGO-Fe_3O_4-PEI-pDNA nanocomposites were fabricated by first chemical depositing Fe_3O_4 onto nGO, and coating branch 25k polyethylenimine (PEI) through electrostatic interaction. By magnetic stirring to enhance the attachment and uptake of functional nGO-Fe_3O_4-PEI nanocomposites on the surface of suspension cells, it was found that the cells showed no significant damage after NIR irradiations at 0.25 mW for 30 min by using calcein-AM & EthD-1 dual staining. The in-vitro study further demonstrated that nGO-Fe_3O_4-PEI-pDNA nanocomposites showed exhibit relatively high gene transfection efficiency and low cytotoxicity on suspension cells (THP-1) in comparison with commercial vector lipofectamine 2000. The experimental results showed that the nGO-Fe_3O_4-PEI nanocomposites can be served as an appropriate non-viral gene vector to treat suspension cells. That means this multifunctional non-viral vector might be probably provided as a transfection tool for stem cell reprogramming.

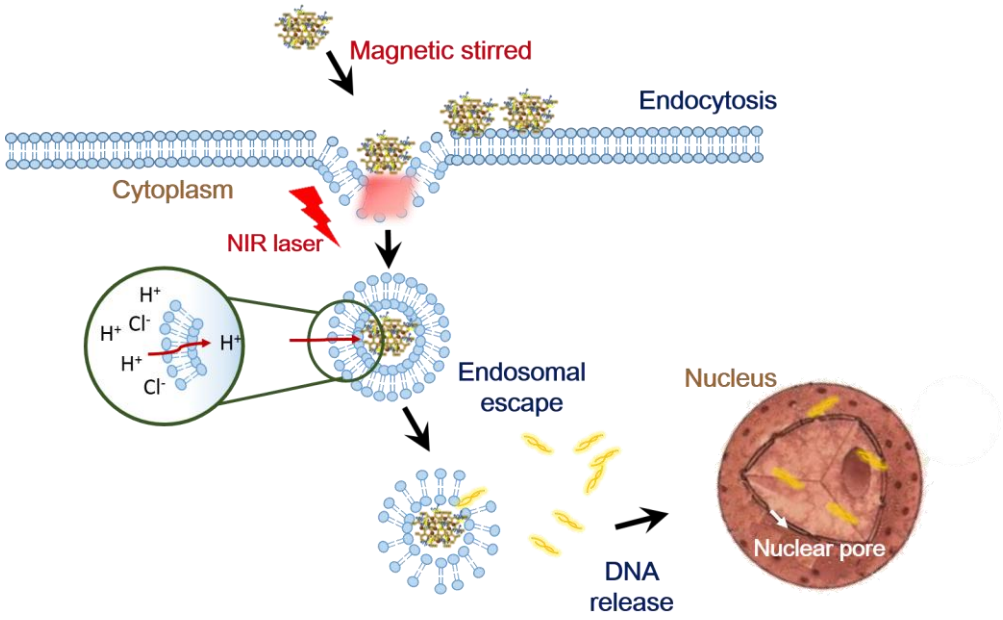

Figure 1. Schematic diagram of intracellular trafficking of non-viral gene transfer nanoparticles.

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PB-13

Effect of Low Temperature Plasma Treatment and UV Light Grafted with Acrylic Acid to Surface of Nano Silver.

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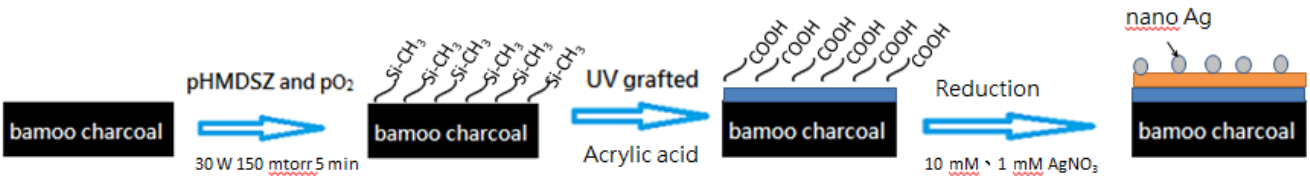
In this study, we use a low temperature plasma process deposition Hexamethyldisilazane (HMDSZ) to surface having hydrophobicity of functional groups and O2 plasma activated surface to having a hydrophilic surface. UV-graft use graft polymerization of Acrylic acid (AAc) on the surface ,then reduces the different concentrations of nano-silver. The method could prepare polymer film containing PAAC nano silver. Bamboo charcoal and PE as substrates. The results shown that the water contact angle of bamboo charcoal increases from 71.6∘to 127.6˚after the HMDSZ plasma processing, and it decreases under 10∘after the O_2 plasma treatment. The particle size of PAAc polymer,nano silver is obtained about 40-80 nm by SEM. ICP detected silver concentration was 9.189 ppm. The different concentration of nano silver can significantly reduce the number of bacteria in antibacterial experiment.



PB-14

Cold Plasma Surface Modified Titanium Alloys Effect of Reduced Graphene Oxide and Graphene Oxide Immobilization on Titanium Implants Improves Osteoblast Growth

Shih-Wen Fang [1], Tse-Ying Liu [1*], Ko-Shao Chen [2 *]
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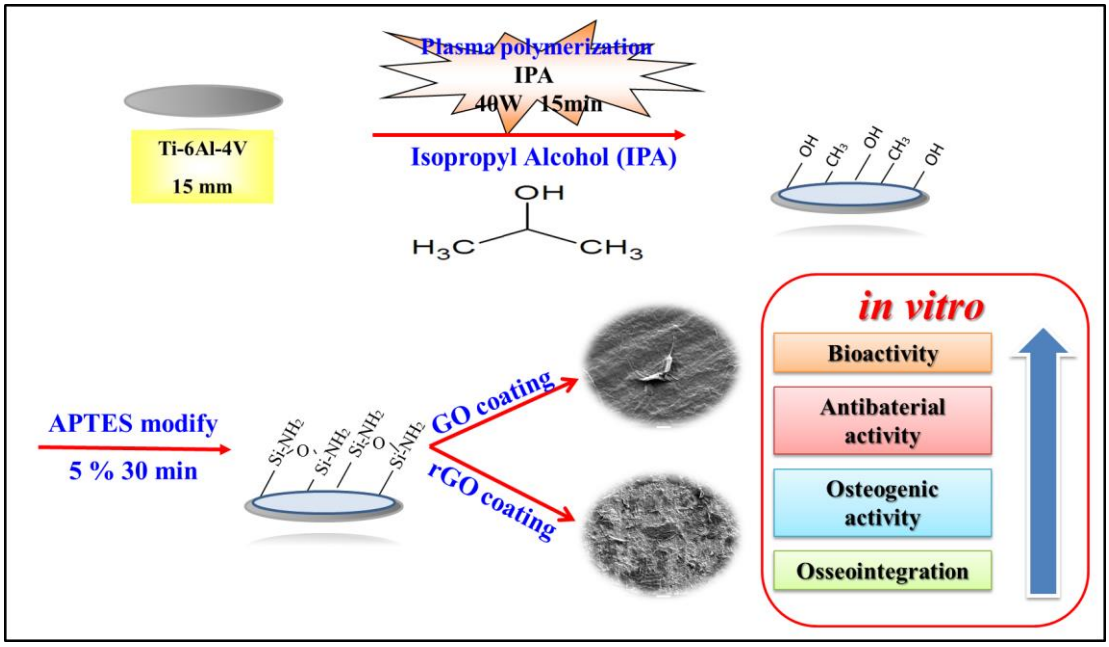
Osseointegration, the formation of a direct interface between an implant and bone without intervening soft tissue, is important for successful bone regeneration and healing in dental and also in orthopedic applications. Dental implants have been widely used in dentistry to replace missing teeth, it made of pure titanium or titanium alloys integrates with the surrounding bone to supports the dental prosthesis. To increased success and predictability of dental implant, many research on the biology of osseointegration and development of modified titanium implant surfaces.

Surface modification of titanium alloys were treatment by isopropyl alcohol (IPA) plasma treatment, then modify the amine group to improve the graphene oxide immobilization on implant surface. Graphene oxide, produced through chemical oxidation and delamination. Due to its hydrophilic property, it can be favorably dispersed in water; therefore, being used in many biomedical applications. Resveratrol (3,5,4′-trihydroxystilbene) is a polyphenol which present in various plants and plant products. It displays multiple biological effects such as cardioprotection, neuroprotection, anti-oxidant, anti-inflammatory, anti-carcinogenic and anti-aging activity. On the other hand, resveratrol not only prevents RANKL-induced osteoclast differentiation, but also improves bone repair by modulation of bone morphogenetic proteins and osteopontin gene expression. The influence on titanium implant were investigated by SEM observations morphology , ESCA analysis surface chemical composition, water contact angle measurements the hydrophilicity and in vitro study was human observed osteoblastic cell growth (MG-63).



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PB-15

Surface Modification of e-PTFE Film by Using Cold Plasma and Graft Polymerization for Immobilization of Biopolymers

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Expanded polytetrafluoroethylene (e-PTFE) is a durable biomaterial and widely used for prostheses in clinical medicine because of its excellent biological inertness (1,2). The aim of this work was to modify the e-PTFE film surface in order to improve its hydrophilicity and biocompatibility. The surface of e-PTFE was activated using low temperature Ar plasma to create active free radicals, and then UV-induced grafting of acrylic acid (AAc) was applied. By the Ar plasma treated for produce on the surface hydrophilic functional groups such as C-O and -COOH, etc. The contact angles of the modified e-PTFE-g-AAc surface film were measured to investigate the variation of surface hydrophilicity. Fourier transform infrared spectroscopy (FTIR) and scanning electron microscope (SEM) were used to respectively observe the chemical structural change and surface morphology of the e-PTFE before and after the modification. After the graft polymerization of AAC on the e-PTFE, biologically compatible substances such as Chitosan and Sodium Alginate were immobilized to the surface through chemical cross-linking with EDC/NHS as bridging agent in order to enhance the biological compatibility (3,4). Cell adhesion test was also conducted in this work for culturing fibroblasts (3T3 Cells) on the immobilized e-PTFE surface. As expected for biomedical drug delivery, artificial dressings, cells or enzymes immobilized value.

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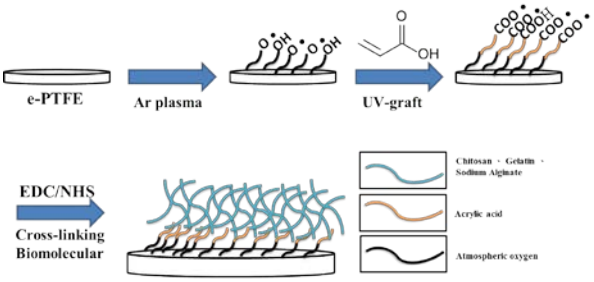
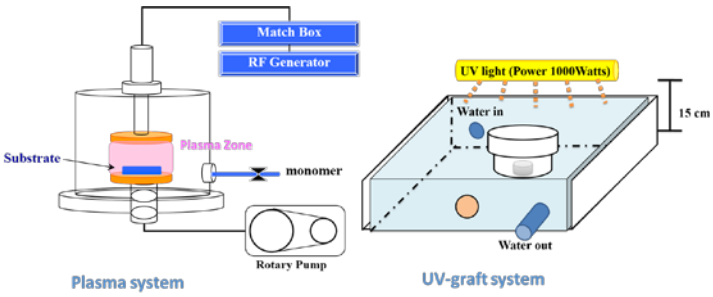
Keywords: Polytetrafluoroethylene, Plasma polymerization, Hydrophilic, AAc, Chitosan

Experiment: flowchart



Schematic diagram



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PB-16

Preparation and Characterization of Polycaprolactone / Cobalt Substituted Hydroxyapatite Nanocomposite Membrane for Bone Regeneration

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Cobalt has been reported to mimic hypoxia, up-regulating hypoxia inducible factor-1α in many different cell types [1]. Ignjatovic N et al show that the cobalt substituted hydroxyapatite with hydrothermal synthesis can promote bone regeneration for osteoporosis rat [2]. In our study, the polycaprolactone (PCL) / cobalt substituted hydroxyapatite (CoHA) nanocomposite was prepared by solvent casting method and oleic acid as surfactant to improve CoHA uniform dispersed in the membrane. Then the influence of the surfactant in characterization of PCL/ Co-HA nanocomposite, including chemical composition, surface morphology, bioactivity and magnetic properties. Synthesis of Co-HA by electrochemical deposition. The electrolyte was prepared by dissolving 42mM calcium nitrate and 25mM ammonium dihydrogen phosphate in distilled water. A quantity of cobalt ion that would allow for 10.6 % (mole %) substitution was added to the electrolyte. The titanium and stainless steel plate were used as a cathode and anode, respectively. The deposition on cathode was cleaned with de-ionized water for several times and dried. ICP-MS results showed that the synthesis of CoHA has the presence of cobalt and substitution percentage is 28.7%. The XRD spectra show an extraneous peak that emerges at about 36.5°, which can likely be assigned to a cobalt oxide phase. Magnetic properties of PCL/CoHA and PCL-OA-CoHA membrane by SQUID analysis at 37°C in a 10 kOe field, as shown in Fig 1. Both PCL/CoHA and PCL-OA-CoHA were shown to have paramagnetic properties by the positive slope of the magnetization-magnetic field curve. In the future will continue to assess whether PCL/CoHA can induce guided bone regeneration at fixed magnetic field.

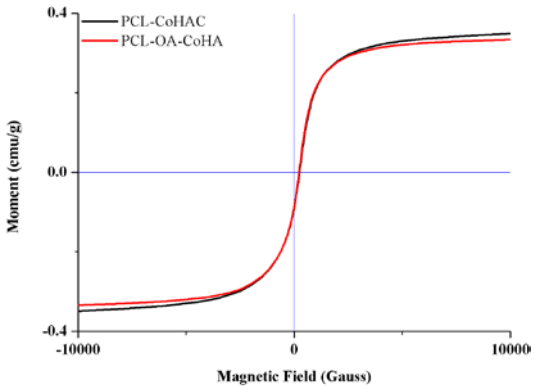

Figure 1. Mass magnetization measurements of PCL-CoHA and PCL-OA-CoHA nanocomposite

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PB-17

Effect of the Surface Properties of Zirconia Post on Bonding Stability of Adhesives

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Clinically, when the teeth pulp necrosis or inflammation, dentist removes the pulp tissue, after root canal debridement and expand, and then do dense root canal filling, and installing crowns, dental patients to relieve pain and cure the root infection tip region. Lack of teeth will support force after root canal therapy, and therefore need additional support since the installation root stem crown. The traditional root stem made of metal or glass fibers, zirconia having high light resistance, aesthetics, good biocompatibility and high tearing resistance and other characteristics, showing the X-ray opacity photography help identify recurrent caries. In our study, the use of different zirconia ceramic discs and cut into a fixed size (10mm x 10mm x 2.5mm) by computer-aided design and manufacturing (CAD/CAM) process, sintered at 1450 °C for 7 hours. The surface roughness and hardness of specimen was analysied. Surface morphology and elemental analysis was obtained by FESEM. The results showed that the surface roughness of the samples ranged from 0.54 to 0.22mm, hardness is 1582 to 1311.7 (see in Table 1). Polygonal grains was found on specimen surface and the size less than 1μm. In result of element analysis shows containing carbon, boron and a small amount of hafnium. Therefore, the sample 1, 3, 4, 6, 7 will be surface modified and evaluate surface properties on the stability of the adhesive by tensile tests[1].

Table 1 Measurement of surface composition and roughness and hardness of different zirconia specimens

Specimen	Company	Surface elemental analysis by EDS					Roughness	Hardness
		B	C	O	Zr	Hf	Ra (μm)	(HV)
1	C	19.87	31.73	37.65	10.75	-	0.54±0.02	1575.6±224.9
2	M	-	-	71.26	27.84	0.38	0.35±0.03	1444.0±101.5
3	N	-	11.02	60.88	27.69	0.41	0.41±0.01	1451.3±182.8
4	U	-	23.60	63.0	13.40	-	0.24±0.04	1363.7±148.8
5	T	-	-	76.84	23.16	-	0.22±0.01	1582.0±140.8
6	T-C	-	14.28	63.90	21.82	-	0.34±0.08	1311.7±128.5
7	T-H	23.11	40.09	31.28	5.52	-	0.26±0.06	1442.8±143.0

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PB-18

Reduced Silver and Graphene Oxide-Based Nanoparticle-Containing Composites by Surface Graft Polymerization of Nano Silver and Graphene Oxide Containing Acrylic Acid

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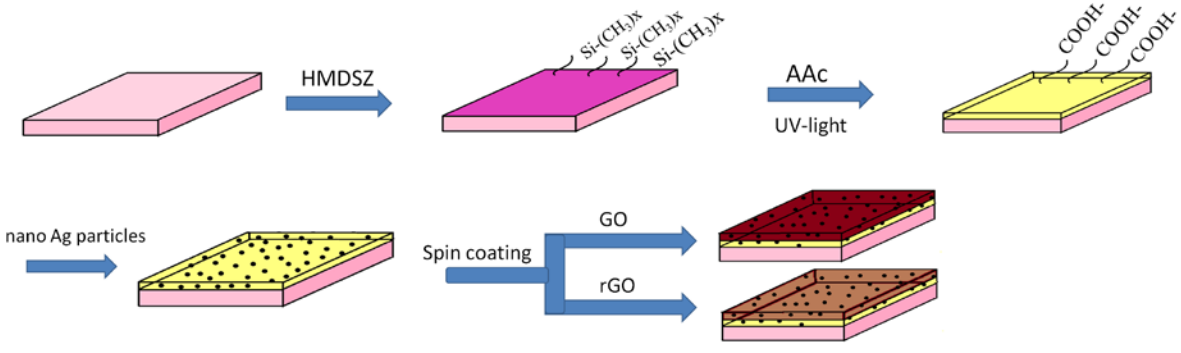
This study use plasma deposition, surface graft polymerization and immobilization to prepare grapheme oxide and nano-silver contained polymeric conductive composites in Al_2O_3 ceramic substrate. Hexamethyldisilazane (HMDSZ) monomer was used to deposit on the substrate to produce an active organic surface film. This surface film is hydrophobic and contains active radicals, which are beneficial for the subsequent graft polymerization. Acrylic acid (AAc) in 6 wt. % was grafted by UV light to the HMDSZ-deposited surface, followed by reduction reaction of sodium borohydride (NaBH4) to immobilize different concentration of nano silver particles on the surface to produce silver-immobilized polymeric conductive composites. The impedance change was measured. The experimental results showed that the impedance of the silver-containing conductive of composites has increase after adding graphene oxide between 18.0%~58.8%.



PB-19

Effect of Atmospheric Plasma Activate Surface and Graft Polymerization of NIPAAm Hydrogel on Deposition of Hydroapatite by Wet Process

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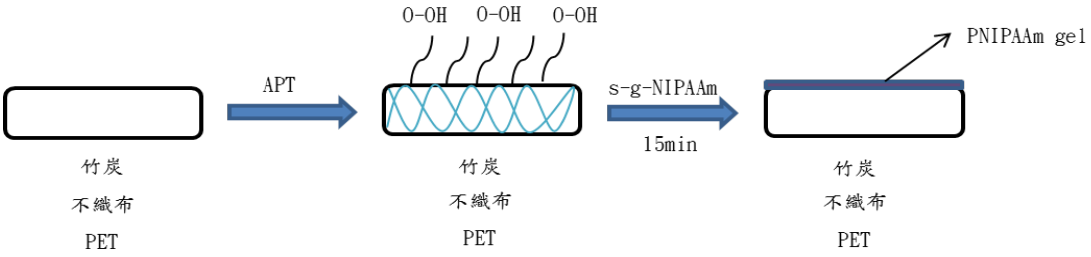
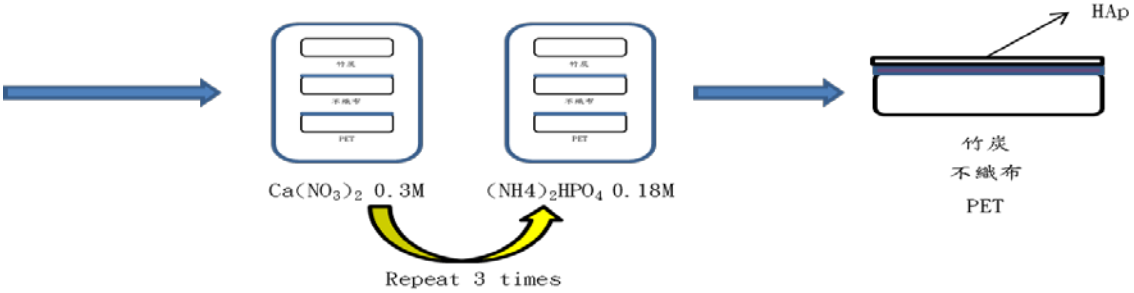
Surface graft polymerization can have pure functional groups in surface which has a wide of applications. In this study He gas atmospheric plasma (voltage: 12,000 V, gas flow rate 0.4 l /min, glow 10mm) treat of polyethylene terephthalate (PET), Bamboo charcoal and TPU nonwoven for surface activate was carry out. We can use the UV-induce graft polymerization of temperature sensitive hydrogel (N-isopropylacrylamide (NIPAAm)) on Plasma activated surface. For deposition of HA we immerse in two separate solution (Ca ion source and Phosphoric ion) for 60 min in each solution per cycle. The results showed that, atmospheric plasma treated substrate, improved the hydrophilic . After treated can success graft poly(NIPAAm) gel on surface . By OM can confirmed the HA formed in surface.

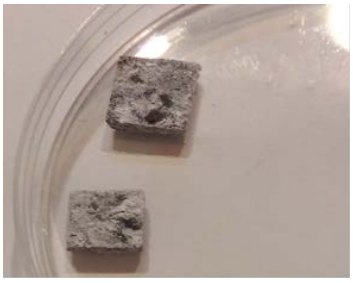
Key word: atmospheric plasma, poly(NIPAAm), Wet process, Hydroapatite

1. Surface modification



2. Wet process for deposition of HA





0m deposition of HA on Bamboo charcoal

PB-20

Cold Plasma Treat Loofah Sponge for Surface Graft and Immobilization of Thermal Sensitive Hydrogel

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Abstract

In this study, Loofah Sponge used as a substrate. Its main component is cellulose with good physical properties .It is able to use in variety of applications by its natural and biodegradable. We modified Loofah cellulose surface to hydrophilic by plasma treatment, and then grafting N-isopropylacrylamide(NIPAAm) or Acrylic Acid(AAc) hydrogel on the surface. It is able to control the amount of grafting polymer by plasma treatment time. Due to temperature sensitive of NIPAAm hydrogel, and the water discharge from the hydrogel by volume shrinkage. The result show that the water discharge rate is about 30% when the loofah cellulose is immersed in hot water. The absorption speed will be longer after treatment by swelling test. We are trying to use Acetic acid plasma treatment after grafting polymer for cell-attached. Because loofah sponge has a large surface area and no toxicity for cell, hoping to use in cultivate in the future.

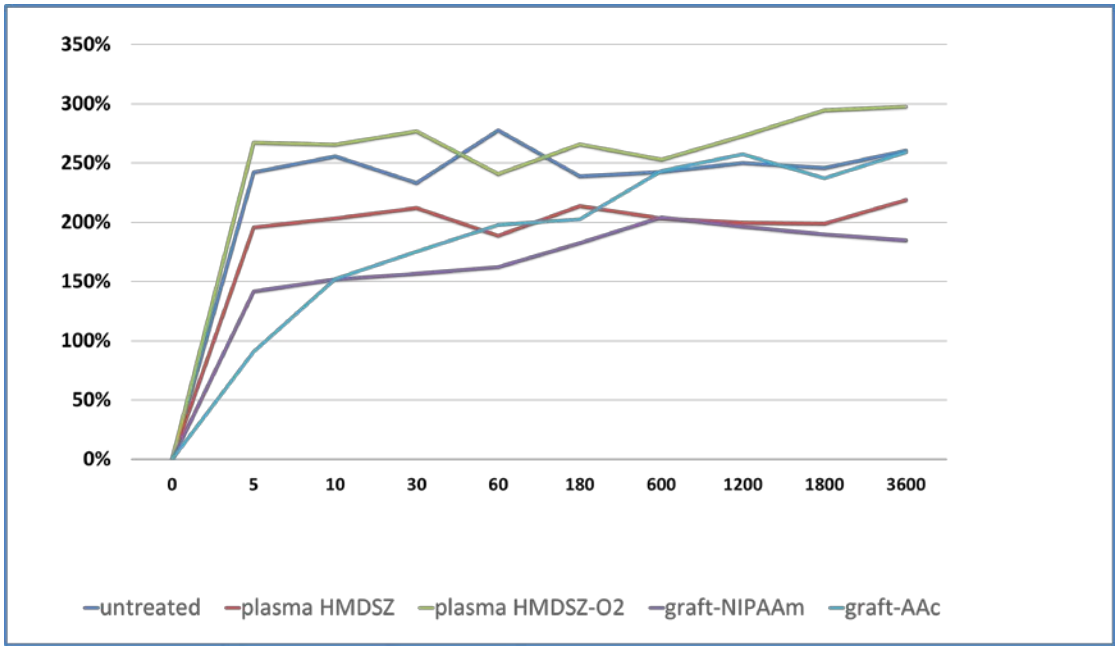

Fig. swelling ratio of modified Loofah Sponge (%)

Keyword: NIPAAm、O_2 Plasma, HMDSZ, Thermal Sensitive Hydrogel, Loofah Sponge

PB-21

A Novel Method to Prepare Biocompatibility and Antimicrobial Polyacrylic Acid/Silver Nanocomposite High-Swell-Ratio Hydrogels

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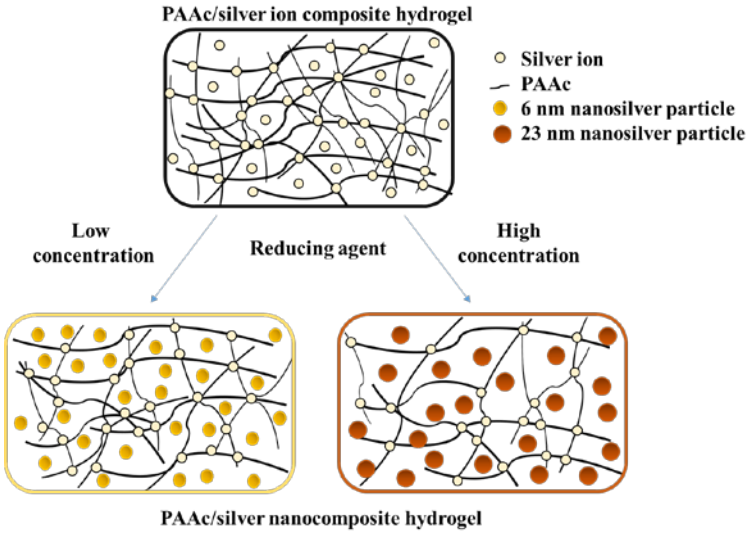
Silver nanocomposites embedded within a polymer matrix have attracted attention in recent years. In this study, we used a solution of the carboxylic monomer acrylic acid and silver nitrate to prepare nanocomposite hydrogels through ultraviolet (UV)-light irradiation. Silver-impregnated biomaterial composed of acrylic acid contains only a monomer and no cross-linker. The formation of hydrogels and reduction of silver nanoparticles were affected by the preparation parameters, that is, the monomer content and silver nitrate concentration. The morphology, structure, and size of the silver nanocomposite hydrogels were evaluated through field emission scanning electron microscopy and UV-visible absorption. The biocompatibility of the samples was tested by A549 cells. The antimicrobial activity of the samples was tested against *Staphylococcus aureus* and *Escherichia coli*. The silver nanocomposite hydrogels contained interior porous structures and open networks of extended honeycomb-like structures, and could absorb 400 to 550 grams of deionized water per gram of dried hydrogel. The silver nanoparticles size was about 5 to 23 nm. Moreover, these hydrogels had a good biocompatibility and strong antibacterial effect, which can be useful in developing new superabsorbent antimicrobial pharmaceutical products.



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PB-22

In Vitro Study of Rat Mesenchymal Stem Cell on Polyelectrolyte Multilayers Coated Ti tanium Alloy

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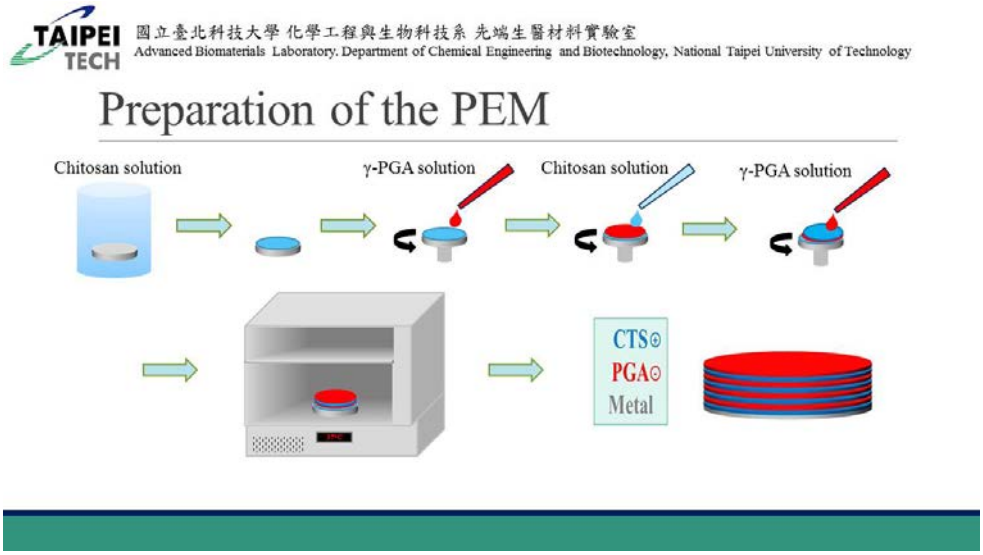
Since titanium alloys have well biocompatibility and proper mechanical properties, they are widely used as orthopedic implants. However, there still remain many problems in clinical, and they lead to transplant failure, causing from incomplete cell attachment, incomplete osseointegration or bacterial infection. In order to solve the problems and improve the surface properties, in this research we prepared polyelectrolyte multilayer (PEM) composed of chitosan and poly-glutamic acid on titanium alloy through spin-coating method, and bone morphogenetic protein 2 (BMP-2) was further loaded. *In vitro* study using SD rat bone-marrow mesenchymal stem cells was carried out to observe the biological effects. The results showed that the PEM treated surface was well biocompatible. Controlled BMP-2 release reached 5 days. Significant osteogenic differentiation was observed comparing to non-treated group at day14. After 21 day co-culture, we found that the calcium content on PEM group was twice more than non-treat group. The results convinced the facilitated cellular mineralization process. Using polyelectrolyte multilayer to improve the surface property and apply for controlled drug release is of great potential.



PB-23

Characterization of near-infrared fluorescent image and photothermal effect of chitosan-based indocyanine green nanocomplexes

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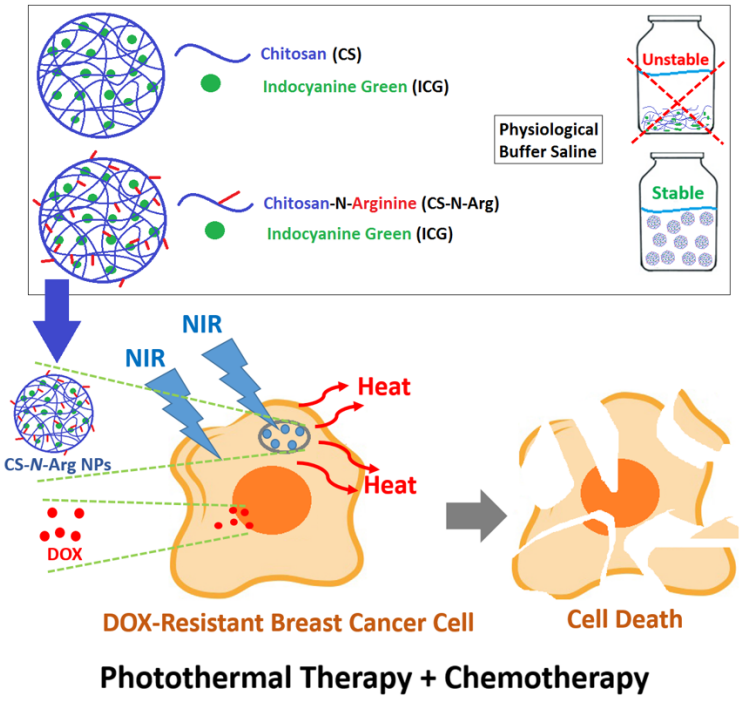
Indocyanine green (ICG) is a Food and Drug Administration (FDA) approved near-infrared (NIR) fluorescent dye which demonstrates great potential in tumor theranostic applications due to its fluorescent imaging and photothermal characteristics. However, the effectiveness of ICG is reduced by its unstable optical property, and concentration-dependent aggregation and precipitation. In this work, we developed a conjugate of chitosan (CS) and arginine (Arg) which could improve the photostability of ICG, thus the CS-*N*-Arg/ICG nanocomplex demonstrated clear NIR fluorescent image and photothermal effect. In combination of doxorubicin (DOX) with CS-*N*-Arg/ICG NPs, a synergistic effect was observed in the DOX-resistant breast cancer cell (MCF-7/ADR) as a result of dual hyperthermia and chemical therapeutic effects.

Keywords: chitosan, arginine, indocyanine green, NIR photothermal



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PB-24

Preparation and in vitro effect of DOX/CuS-loaded EGCG/GN NPs on breast cancer cells

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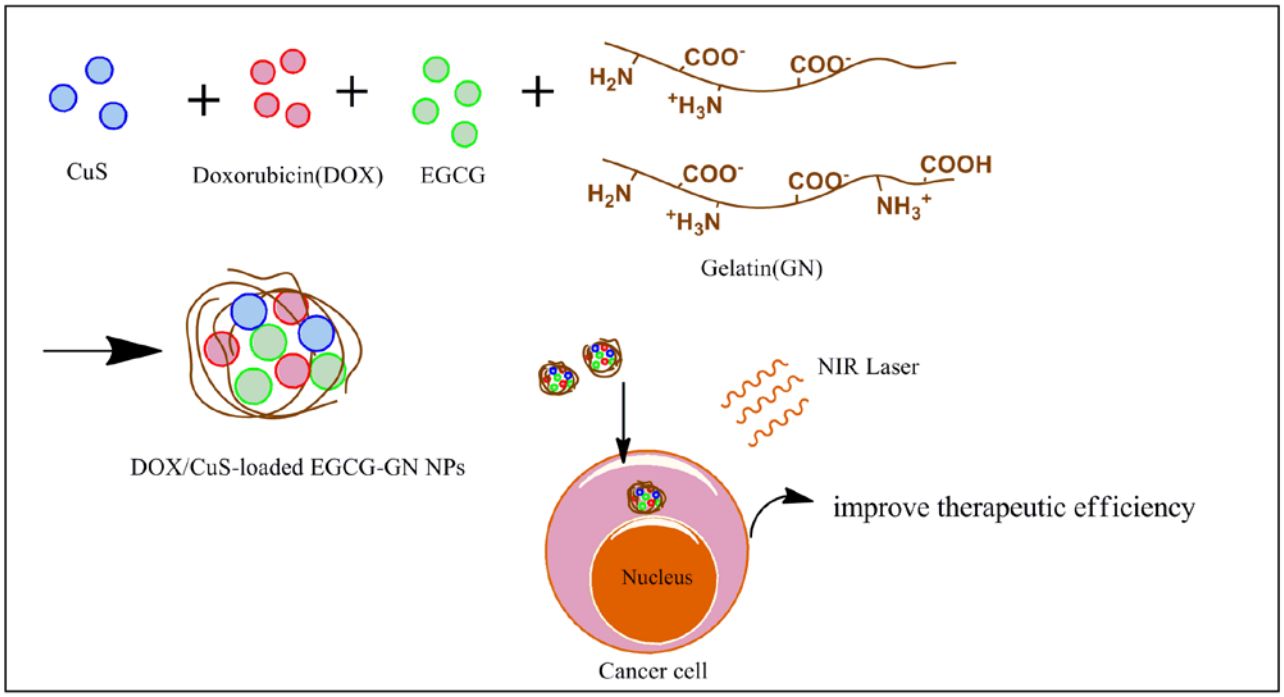
A combination of chermotherapy and photothermal therapy has become a promising treatment against cancer. Herein, we fabricated doxorubicin (DOX) and copper sulfide (CuS) loaded gelatin (GN) /epigallocatechin-3-gallate (EGCG) nanoparticles using self-assembly method. CuS obtained by the reaction of copper(II) chloride with sodium sulfide in the presence of sodium citrate display strong absorption peak at 980 nm in the near-infrared (NIR) region. The hybrid nanoparticles were characterized by dynamic light scattering, transmission electron microscopy, UV-Vis absorption spectra, Fourier transform infrared spectroscopy, and the photothermal effect was investigated under 980 nm NIR irradiation. The in vitro anticancer effects of the hybrid nanoparticles were examined by chermotherapy, photothermal therapy, and chermo- and photothermal combined therapy using MCF-7 cell lines.



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PB-25

Photothermal Tumor Ablation in Mice with Repeated Therapy Sessions Using NIR Absorbing Micellar Hydrogels Formed In Situ

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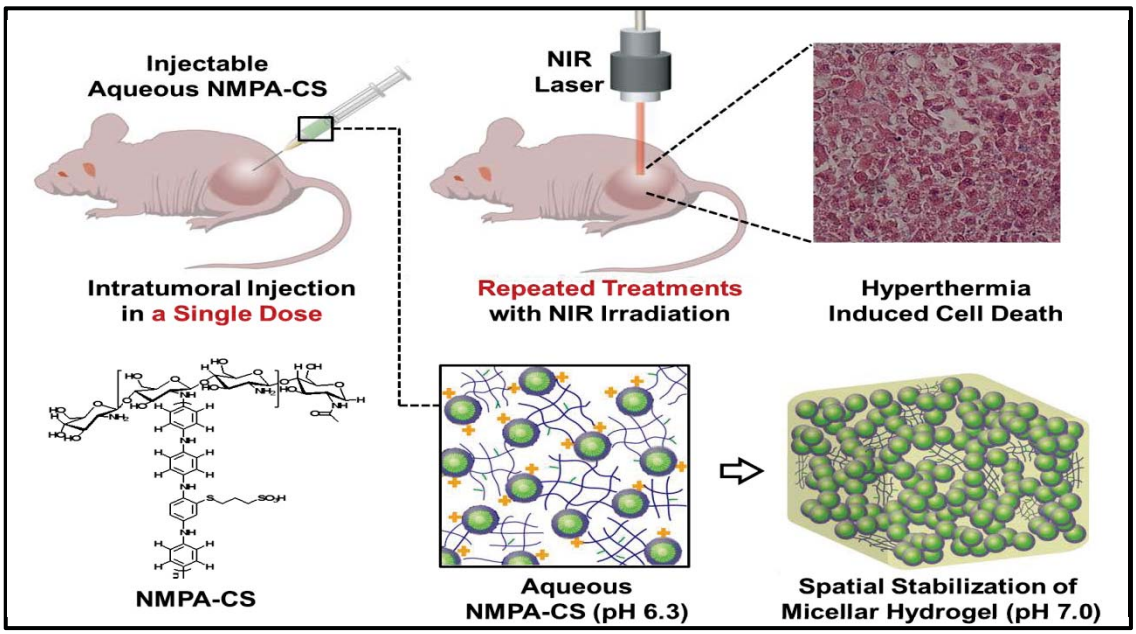
Repeated cancer treatments are common, owing to the aggressive and resistant nature of tumors. This work presents a chitosan (CS) derivative that contains self-doped polyaniline (PANI) sidechains, capable of self-assembling to form micelles and then transforming into hydrogels driven by a local change in pH. Analysis results of small-angle X-ray scattering indicate that the sol-gel transition of this CS derivative may provide the mechanical integrity to maintain its spatial stability in the microenvironment of solid tumors. The micelles formed in the CS hydrogel function as nano scaled heating sources upon exposure to near-infrared light, thereby enabling the selective killing of cancer cells in a light-treated area. Additionally, photothermal efficacy of the micellar hydrogel is evaluated using a tumor-bearing mouse model; hollow gold nanospheres (HGNs) are used forcomparison. Given the ability of the micellar hydrogel to provide spatial stability within a solid tumor, which prevents its leakage from the injection site, the therapeutic efficacy of this hydrogel, as a photothermal therapeutic agent for repeated treatments, exceeds that of nanosized HGNs. Results of this study demonstrate that thisin situ-formed micellar hydrogel is a highly promising modality for repeated cancer treatments, providing a clinically viable, minimally invasive phototherapeutic option for therapeutic treatment.



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PB-26

Targeted Therapy with Spatially and Temporally Precise Controlled Release Using a FRET-guided, NIR-responsive Bubble-generating Liposomal System

Ching-Hua Chiang [1], **Er-Yuan Cuang**[1], **Chia-Chen Lin**[1], **De-Hui Wan**[2], **and Hsing-Wen Sung***[12]
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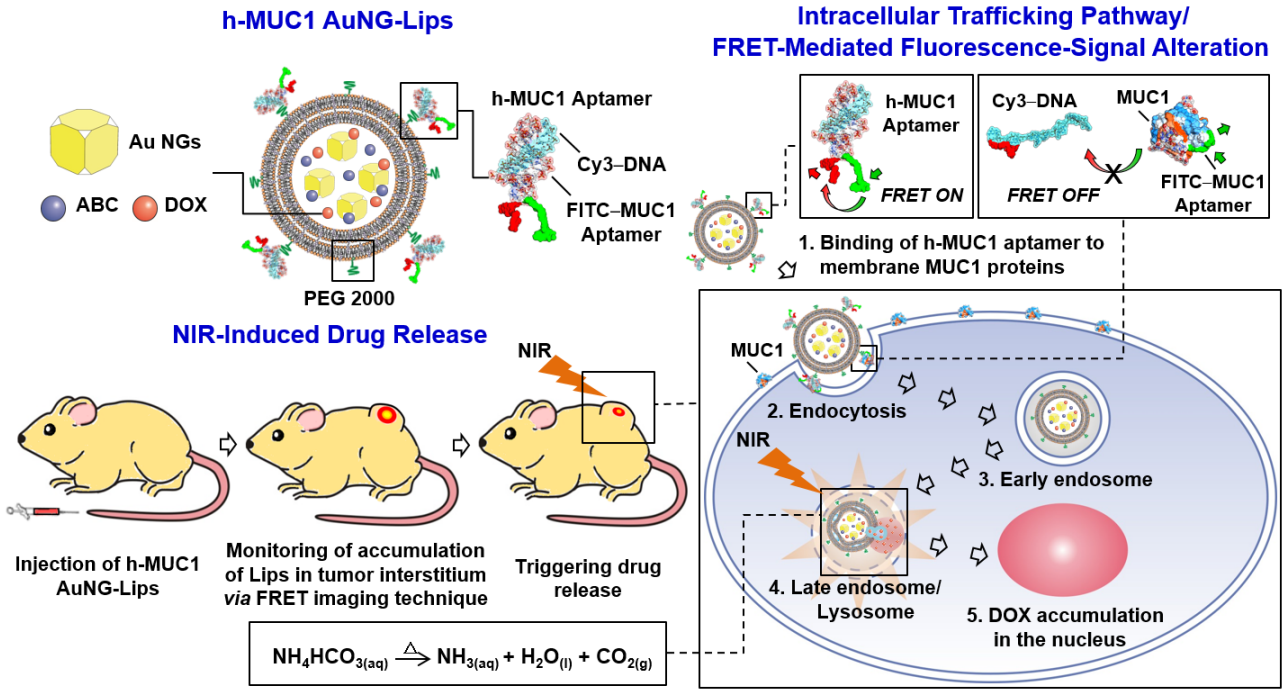
The nonspecific distribution of therapeutic agents and nontargeted heating commonly produce undesirable side effects during cancer treatment since the optimal timing of triggering the carrier systems is unknown. This work proposes a multifunctional liposomal system that can intracellularly and simultaneously deliver the therapeutic drug doxorubicin (DOX), heat, and a bubble-generating agent (ammonium bicarbonate, ABC) into targeted tumor cells to have a cytotoxic effect. Gold nanocages that are encapsulated in liposomes effectively convert near-infrared light irradiation into localized heat, which causes the decomposition of ABC and generates CO2 bubbles, rapidly triggering the release of DOX. Additionally, a hybridized Mucin-1 aptamer is conjugated on the surface of the test liposomes, which then function as a recognition probe to enhance the uptake of those liposomes by cells, and as a molecular beacon to signal when the internalized particles have been maximized, which is the optimal time for photothermally triggering the release of the drug following the systemic administration of the liposomes. Empirical results reveal that this combined treatment effectively controls targeted drug release in a spatially and temporally precise fashion and so significantly increases the potency of the drug while minimizing unwanted side effects, making it a promising treatment for cancer.



PB-27

Assembling Composite Dermal Papilla Spheres with Adipose-derived Stem Cells to Enhance Hair Follicle Induction

Tzu-Chieh Huang[1], Ya-Ju Chang[1], Yuan-Yu Hsueh[3], Fong-Chin Su[2], Cheng-Ming Chuong[4,5,6], Chia-Ching Wu*[1,2,4,5]

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The microenvironmental interaction between dermal papilla (DP) cells and intradermal adipose tissue within hair follicles is essential for promoting hair neogenesis. However, the precise interaction of adipose-related cells for better hair follicle function are poorly studied. In our lab, we were able to culture DP cells in three dimensional structure by forming DP spheres in unite size and modulate sphere characteristics through involvement of adipose-derived stem cells (ASCs). The study aims to investigate the cell interaction of DP and ASCs in various assembly strategies for facilitating hair formation. To reconstruct hair follicles, we seeded DP on chitosan-coated surface to form spheres. Besides, ASCs were co-cultured with DP by different assembling approaches; a mixed sphere of ASCs with DP cells (MA-DPS), or a core-shell structure, outer ASCs shell and an inner DP core (CSA-DPS). CSA-DPS provided superior microenvironment cuing to maintain the expression of DP marks compared to MA-DPS. ASCs, but not differentiated adipocytes, further promoted DP markers and functional alkaline phosphatase activity of the DP cells. The in vivo patch assay demonstrated that CSA-DPS developed into hair-like structures which could barely be found in MA-DPS treatment. Through cell tracing technique, we observed that the core-shell structure of CSA-DPS showed the ability to trap ASCs and promoted PPARα signal in ASCs to induce the greater hair induction than MA-DPS. In conclusion, ASCs exhibited great potential to promote hair follicle function through PPARα pathway. Furthermore, core-shell structure provide a suitable microenvironment to facilitate cell interaction between DP and ASCs.

PB-28

Resveratrol-loaded nanoparticles improve the sensitivity of doxorubicin and its anti-inflammatory effect

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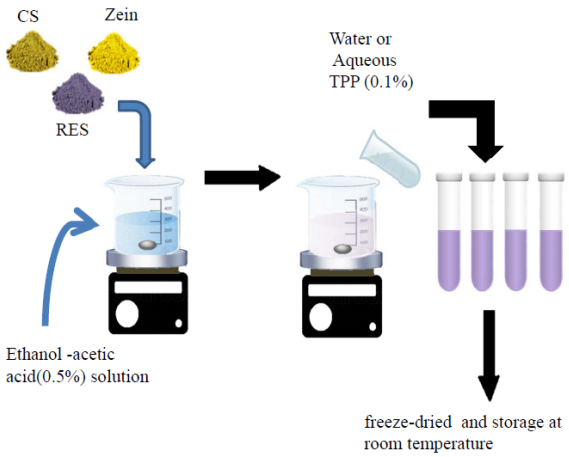
Abstract

Resveratrol offers pleiotropic health benefits including anti-inflammatory, antioxidant, cardio protection and anticancer activities. However, the clinical use of resveratrol has been limited by its high lipophilicity, short biological half-life, and chemical instability. Zein is the major storage protein in corn which demonstrates inherent free radical scavenging activity. The objective of this work was to synthesize a chitosan-zein (CS-Zein) conjugate which can effectively encapsulate resveratrol through the formation of self-assembled nanoparticles. CS-Zein/resveratrol colloidal nanoparticles (CS-Zein/RES NPs) were stable in water, and their free radical scavenging and anti-inflammatory activities were excellent as estimated by free radicals scavenging and nitric oxide (NO) inhibition assay. CS-Zein/RES NPs also increased the sensitivity of DOX on multidrug-resistant breast cancer cells (MCF-7/ADR).



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PB-29

A Study on Effects of The Monomer Content, Photocuring Time and Visible-Light Intensity in Cured Resins of Bis-phenol A Diglycidyl Methacrylate and Triethylene Glycol Dimethacrylate

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Adhesives were prepared by using various mole ratios of bis-phenol A diglycidyl methacrylate（BisGMA）(50~80 mol%) and triethylene glycol dimethacrylate (TEGDMA) (20~50 mol%) in feed, with camphorquinone (CQ) and diphenylphosphine oxide as the photoinitiators. We use the different photocuring times (2~6 mins) and different light intensities (600~1800 mW/cm^2) of visible light. We examine the effects of BisGMA/TEGDMA mole ratios in feed, photocuring times and light intensities on conversion of reaction, and how crosslink density and conversion of reaction affect the interactions between water and polymers in swollen resins and dynamic mechanical properties of dry resins.

According to FTIR analysis, as the contents of BisGMA increase, the photocuring times increase or the light intensity increases, the conversions of double bonds increase. There is a power raw relationship between the conversion and light intensity with an exponent equal to 0.226~0.371. The order of propagation reaction (n) and reaction rate constant (k) are calculated by the conversions of double bonds versus photocuring times. As the contents of BisGMA increase or the light intensity increases, both of the n values and k values decrease. Compressive modulus and crosslinking density increase with increasing the contents of BisGMA in feed. Both of the density of physical entanglement（N_s）and the density of chemical crosslinking in network（N_c） increase with increasing the contents of BisGMA in feed, showing that adding BisGMA is favorable for physical and chemical crosslinking. And increasing the photocuring times or the light intensities, leads to similar results to the above. In addition, the interaction parameters of water and polymers in adhesives (χ) were calculated by crosslinking densities and equilibrium water contents. As the contents of BisGMA increase, the photocuring times increase or the light intensity increases, the χ values increase and the equilibrium water contents decrease. Curing volume shrinkages decrease with increasing the contents of BisGMA in feed or increasing the light intensity because of BisGMA with benzene structure offering the less shrinkage than TEGDMA. But increasing the photocuring times, the curing volume shrinkages increase. According to DMA analysis, as the contents of BisGMA increase, the photocuring times increase or the light intensity increases, the storage modulus and the glass transition temperature (T_g) will increase. The glass transition temperature is increased by increasing crosslink density, there is a linear relationship between them. And there is a power raw relationship between the storage modulus and crosslink density with an exponent equal to 1.918.

Experimental results show that we vary BisGMA/TEGDMA ratios in feed, photocuring times or light intensities, that will influence the conversions of double bonds, network structure of polymer and crosslink density, thereby affecting the interactions between water and polymers in swollen resins, as well as affecting dynamic mechanical properties of dry resins.

PC-1

Development and Characterization of Swellable and Bioadhesive Gastroretentive Drug Dosage Form (*sb*GRDDF) Composed of Polyelectrolyte Hydrogel of Chitosan with ring-opened Polyvinyl Pyrrolidone (*ro*PVP) for Improving Oral Bioavailability of Alendronate

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A novel GRDDF (Gastroretentive Drug Dosage Form) system could not only sustain release of drug but also increase the residence time of the drug in stomach by three retentive mechanisms of swelling, floating and bioadhesion. Alendronate preferably absorbed from upper gastrointestinal tract was selected as the model drug. The aim of this study was to prepare and characterize a swellable and bioadhesive gastroretentive drug dosage form (*sb*GRDDF) based on the complex hydrogel formed between chitosan (CS) and ring-opened polyvinyl pyrrolidone (*ro*PVP) via charge interaction
The complex hydrogel of CS/*ro*PVP was produced by blending CS (cation) with *ro*PVP (anion) obtained by basic treatment.

The influence of heating time and NaOH concentration for preparing *ro*PVP, different MW of CS, and different ratio of CS/*ro*PVP on the swelling ability of resultant complex hydrogel was characterized and optimized. Results demonstrated that *ro*PVP in 0.5M sodium hydroxide solution with a 4h-heating at 50℃ had the optimal property for preparing complex hydrogel with CS. However, there showed an insignificant influence of different Mw of CS, different ratio and different tableting pressure on the swelling ratio. Among all, the complex hydrogel formed with high Mw chitosan and *ro*PVP at 1:20 weight ratio possessed the optimal swelling ability in Fig1(A). In vitro dissolution test,Fig1(B) showed optimized formulation reveals that the drug released slowly and constantly. In vivo pharmacokinetics study further, Fig1(C) demonstrated that the oral bioavailability of alendronate was enhanced three folds and the mucosa irritation was reduced.

In conclusion, *sb*GRDDF composed of CS/*ro*PVP complex hydrogel was successfully developed and is potentially applicable to improve clinical efficacy of bisphosphonates with minimization of side effects.

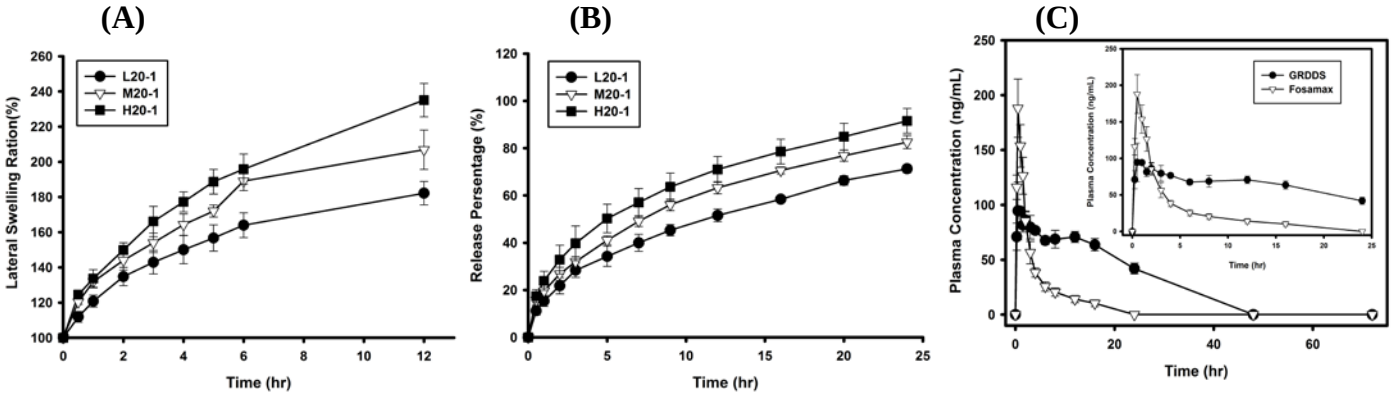

Figure 1. Lateral swelling ability of (A) and dissolution profile of alendronate in SGF from (B) tablets prepared with *ro*PVP/CS hydrogels composed of *ro*PVP complexed with either low MW chitosan, medium MW chitosan, or high MW chitosan at a *ro*PVP:CS ratios of 20:1. (C) Plasma alendronate concentration profiles after administration 72 hr of different alendronate formulations. (mean ± S.D., n=3)

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PC-2

Development and Characterization of Lecithin-based Self-Assembly Mixed Micellar Drug Delivery Systems for Curcumin

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Curcumin is the active ingredient extracted from the root of Curcuma longa. The great therapeutic applications of curcumin are restricted because of its low aqueous solubility, light instability and hydrophobic character, resulting in poor bioavailability (BA). Mixed polymeric micelles (MPM), which is able to increase the volume of the hydrophobic core by incorporating extra hydrophobic materials providing larger space for hydrophobic drugs to be solubilized, was developed to overcome major obstacles associated with curcumin delivery.

Self-assembling curcumin-MPM prepared by thin film method was evaluated to assess characteristics such as the average particle size and size distribution, encapsulation efficacy (EE) and drug loading (DL). After optimization, the formulations were composed of curcumin/lecithin/NaDOC= 2/1/5 and curcumin/lecithin/Pluronic® P123=5/2/20, with particle size of < 200 nm, EE of >80%, and DL of >10%. The optimized formulation improved the stability of curcumin in PBS at room temperature or 4 ℃, and in FBS or PBS at 37℃, and retarded in vitro curcumin release. In vivo PK studies shows for oral administration, the absolute BA was 3- and 5-fold increased for curcumin-loaded NaDOC and Pluronic® P123 MPM, respectively; for intravenous administration, the absolute BA was 2.32- and 5.73-fold improvement for curcumin-loaded NaDOC MPM and Pluronic® P123 MPM, respectively.

In conclusion, lecithin-based MPM represented a useful curcumin delivery system, thereby improving the solubility, stability and BA of curcumin. The enhancement of curcumin BA via lecithin-based MPM can bring this natural molecule to the forefront of therapeutic agents which can treat dreadful cancer.

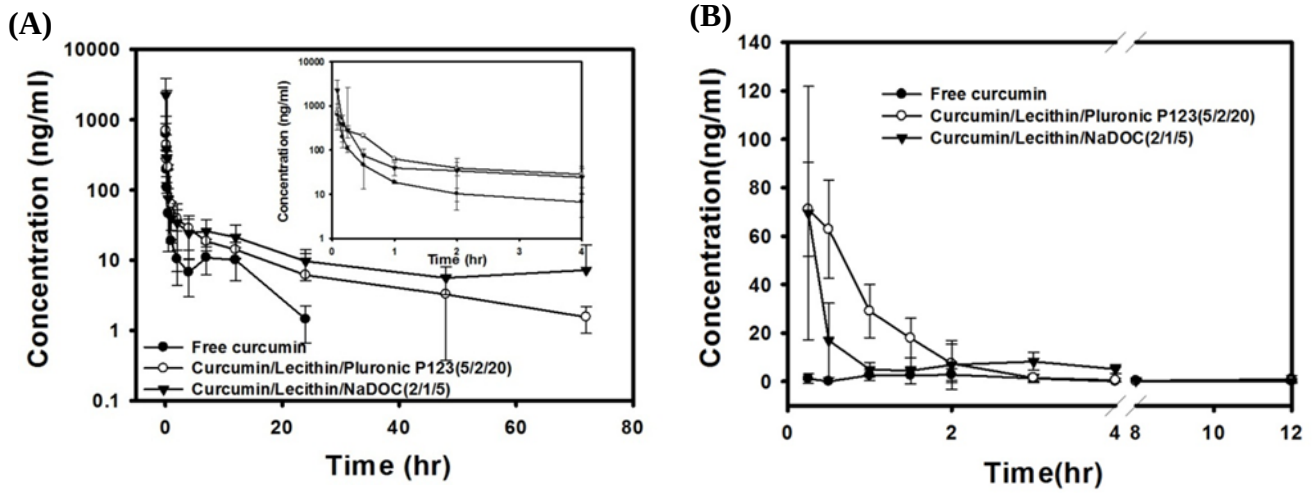

Figure 1. (A) Plasma concentration-time curves of curcumin after intravenous administration of lecithin-based mixed micelles (NaDOC and Pluronic® P123) and free curcumin (5 mg/kg) to rats. (B) Plasma concentration-time curves of curcumin after oral administration of lecithin-based mixed micelles (NaDOC and Pluronic® P123) and free curcumin (100 mg/kg) to rats. (mean ± S.D., n=3)

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PC-3

Preparation of albumin-bound nanoparticles by two steps emulsification

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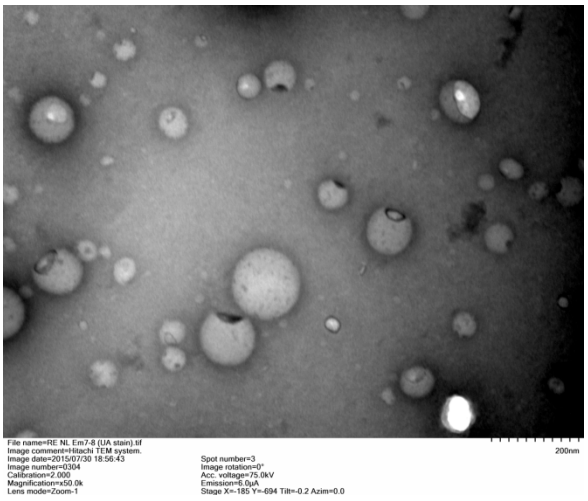
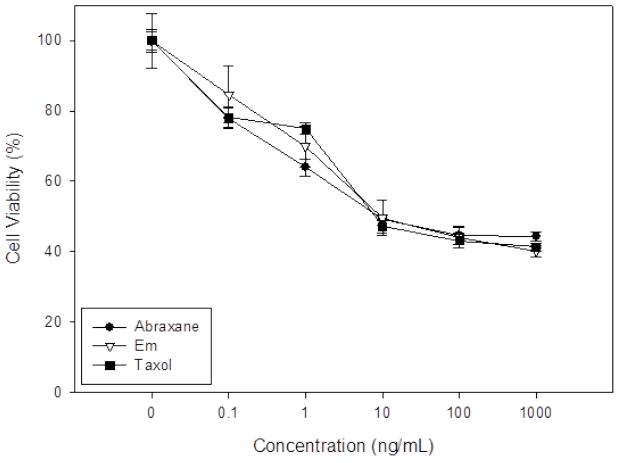
Improving the balance between efficacy and toxicity of anticancer drug is still the challenge. Since albumin permeate into interstitium through leaky blood vessels and enhanced retention in tumor tissue by the lack of lymphatic systems. In addition, hydrophobic drugs encapsulated into water soluble albumin can eliminate the usage of surfactants in the dosage form. Therefore, albumin nanoparticles have the chance to solve the challenge. High energy emulsification approaches such as high pressure homogenizer and ultrasonicator have been applied to produce the drug loading albumin nanoparticles. In the present study, chloroform dissolved with paclitaxel was emulsified into the albumin solution by ultrasound. The primary emulsion was sequentially emulsified through high pressure homogenizer. The final emulsion was rotary-evaporated under reduced pressure, and then lyophilized. The following factors are examined, the temperature of albumin solution (10°C and room temperature), the ratio of organic solvent to albumin solution (1.25%, 3%, 5%), the distance between the ultrasound tip and the base of the reaction chamber (19 and 38 mm), ultrasonication amplitude (30%, 50%, 75%), ultrasonication time (1 to 5 minutes). Through the two steps emulsification, the encapsulation efficiency of paclitaxel in albumin nanoparticle could be enhanced from 29.8% to 80.4% compared with the ultrasonic emulsification only. The particle size of albumin nanoparticles produced by two processes was similar and around 200 nm. Comparing the efficacy and toxicity through MTT cell viability test and maximum tolerated dose study, albumin nanoparticles manufacturing by two steps emulsification had the similar results with commercial product Abraxane®. The results demonstrated that for albumin nanoparticles, the goal of better drug encapsulation efficacy, high anticancer efficacy and low toxicity were achieved by the two step emulsification without using additional stabilizer.



Transmission electron microscopy (TEM) micrograph of albumin nanoparticles prepared by two steps emulsification.



Effect of albumin nanoparticles prepared by two steps emulsification (Em), Abraxane® and Taxol® on MDA-MB-231 viability.

PC-4

Development and Characterization of Lecithin-based Micellar System for Quercetin and Its Study of Pharmacokinetics and Anti-cancer Effect

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Quercetin (3,3',4',5,7-pentahydroxyflavone) has been intensively investigated for anti-inflammatory, antioxidant, antiviral, and anti-carcinogenic properties. The use of the quercetin as a therapeutic agent is largely hampered due to its poor water solubility, short biological half-life and low oral bioavailability. This study sought to develop a lecithin stabilized micelle encapsulating quercetin. An optimal formulation composed of quercetin: TPGS: Lecithin in a 6:40:80 weight ratio was obtained, with a high drug loading of 4.7%, a minor particle size of 92.2nm, and prepared by thin-film hydration method. The results of quercetin release from micelle formulation was slower than free quercetin in phosphate buffer (pH 7.4 PBS) with 0.5% Tween 80 at 37°C. A cytotoxicity assay revealed that quercetin micelles had significant anticancer activities against MCF7, SKBR3, MDA-MB-231 human breast cancer cell and CT26 mouse colon cancer cell. The tumor inhibiting ability of lecithin stabilized micelle was confirmed by in vivo tumor-bearing (CT26 colon cancer cell) mice. It was observed that lecithin stabilized micelle were successfully accumulated by tumor tissues in tumor-bearing mice, because of the prolonged circulation and enhanced permeability and retention (EPR) effect. In pharmacokinetics study, intravenous and oral administration of quercetin lecithin stabilized micelles was found to significantly increase the relative bioavailability to 158 % and 360 %, respectively and absolute oral bioavailability to 5.13 %. In addition, the effect of doxorubicin in combination with quercetin resulted in efficient growth inhibition of CT26 colon cancer cell and reduced cardiac toxicity on Balb/c mice model.

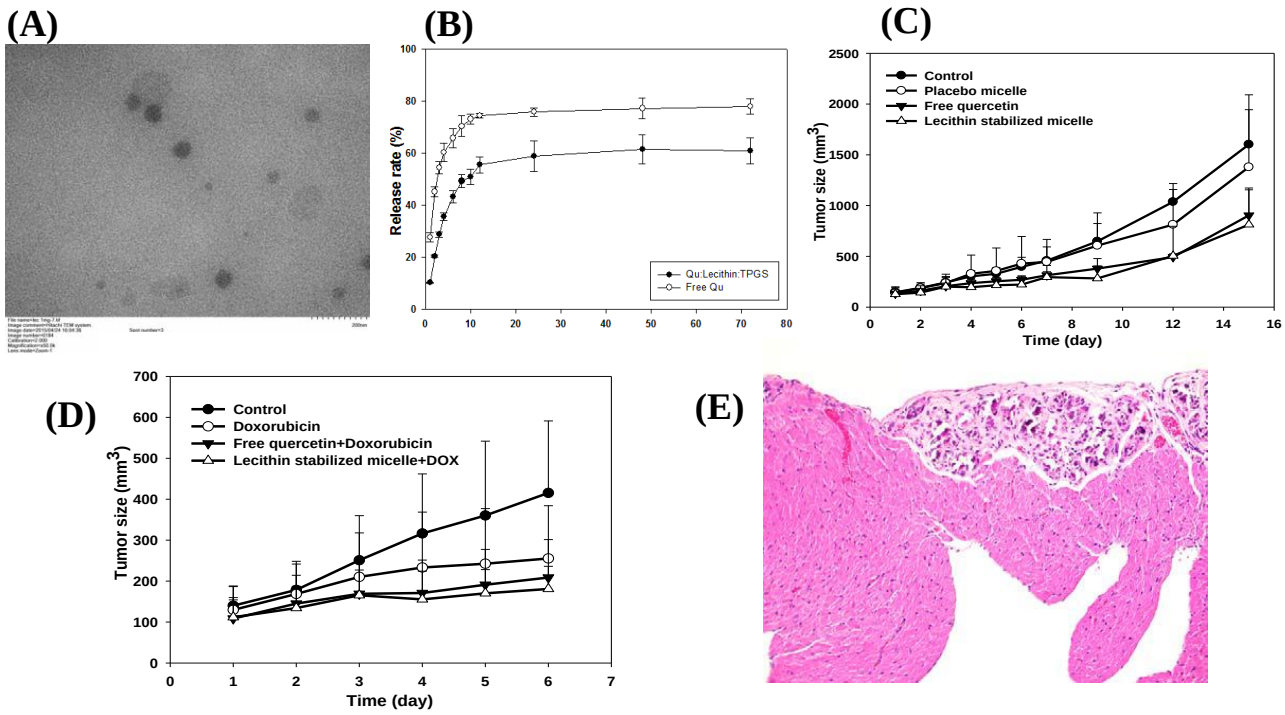

Figure (A) TEM photographs of M-DocLF at 50K magnification. (B) Drug release profile of free quercetin and lecithin stabilized micelles in pH 7.4 phosphate buffer with 0.5 % Tween 80 (C)Changes in tumor volumes after injection of PBS, placebo lecithin stabilized micelles, quercetin lecithin stabilized micelles in Q1d*7 50 mg/kg, respectively. (D) Changes in tumor volumes after injection of PBS, doxorubicin, quercetin lecithin stabilized micelles plus doxorubicin, free quercetin plus doxorubicin in Q1d*5.Quercetin in 50 mg/kg and doxorubicin in 4 mg/kg, respectively. (E) Photographs of histopathology examination after injection of Lecithin stabilized micelles plus doxorubicin in day3

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PC-5

PCOX Microneedles Containing Gelatin Microspheres as a Dual-Drug Release System for Transdermal Delivery of Hydrophilic and Lipophilic Drugs

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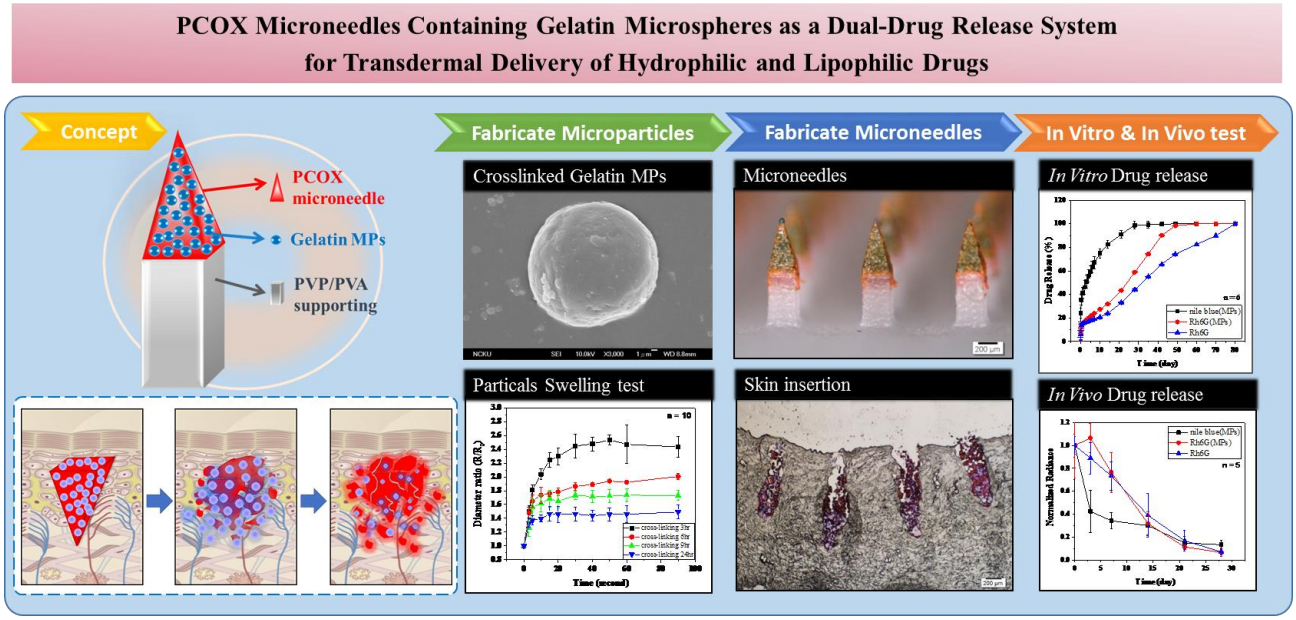
This study reports embeddable polycarbonate-co-polyoxalate (PCOX) microneedles (MNs) containing crosslinked gelatin microspheres (MPs) as a dual-drug transdermal delivery system for hydrophilic and hydrophobic drugs. In this system, hydrophobic model drugs, rhodamine 6G (rh6G), was encapsulated within the MNs; whereas hydrophilic model drugs, nile blue, was loaded within the MPs. PCOX MNs were mounted to the top of a dissolvable poly(n-vinylpyrrolidone)/poly(vinyl alcohol) (PVP/PVA) supporting array, providing mechanical strength to fully insert the MNs into the skin. When inserted into the skin, the supporting array can be quickly dissolved by interstitial fluid, leaving the MNs within the skin for sustained drug delivery without requiring a transdermal patch. The gelatin MPs quickly swell to release nile blue because of contact with skin's water. Such swelling will cause the MN disintegration, thus accelerating rh6G release from the MNs. When contact with water for 90 s, the diameter of the crosslinked gelatin MPs can swell to ~2 times their initial diameter (n = 10). These MNs can be inserted into porcine and rat skins at a depth of 700~1000 μm. *In vitro* drug release study showed nile blue can be quickly released from the MNs (~80% at Day 14). At Day 50, 100% of rh6G was released from the group with MPs, whereas there is only 75% of rh6G release from their counterpart. Such release behavior can be also observed from the *in vivo* drug release study. These results demonstrated that the embeddable PCOX MNs with gelatin MPs may be a new generation of transdermal delivery system.



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PC-6

Fabricating Multifunction PLGA NPs Reducing for Reperfusion Injury of MI Heart

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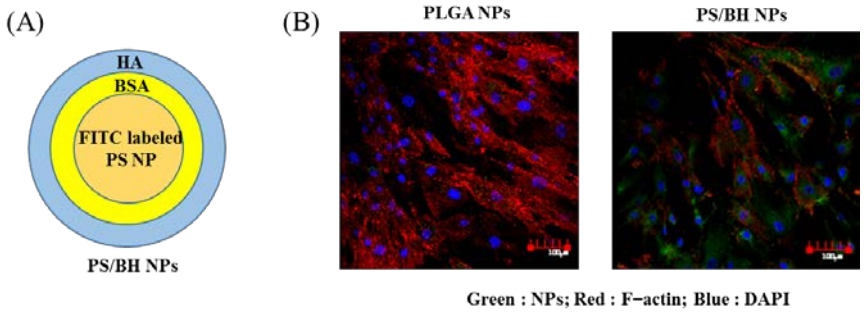
Reperfusion of myocardial infarction (MI) would cause myocardial injury. CyA is a drug that inhibits opening of MPT pores which could reduce cardiomyocyte apoptosis; hirudin (HD) is an anti-thrombin drug which reduces blood coagulation factors to induce apoptosis of cardiomyocytes; GSH is a peptide with anti-oxidation property. In this study, we developed FITC labeled PLGA-SA nanoparticles (PS NPs) for CyA delivery. NPs were coated by HD and HA (H) on NP surfaces using the layer-by-layer technique to fabricate fluorescent, anti-coagulation with long circulation and hBMSC-targeting multifunction NPs. HD was replaced by BSA (B) at present study. PS NP with size of 251.4 ± 3.2 nm with zeta potential of +24.9 ± 2.1 mV, and 294.7 ± 9.1 nm and -6.7 ± 0.7 mV for PS/BH NPs. The components of NPs were confirmed by FTIR and TEM. The accumulative release of CyA and BSA, which reached 36.7% and 29.8%, at 8hr separately; and 46.4% and 44.8% at 72hr. Uptake of PS/BH NPs by hBMSC were 20.3% more than that of PLGA NPs, revealing the hBMSC-targeting property was demonstrated. Additionally, anti-oxidation effect of PS/BH NPs containing GSH was verified by an oxidation of SF gelation model. PS/BH or PS/HDH NPs containing GSH exhibit multifunction fluorescence, anti-coagulation or anti-oxidation properties could have potential used for reducing reperfusion injury of MI.

(A) PS/BH NPs; (B) Various NPs uptake by hBMSC at 1hr.



PC-7

PLGA/SA Based Multifunctional NP/hBMSC Delivery System for Reducing Oxidative Injury of MI Heart

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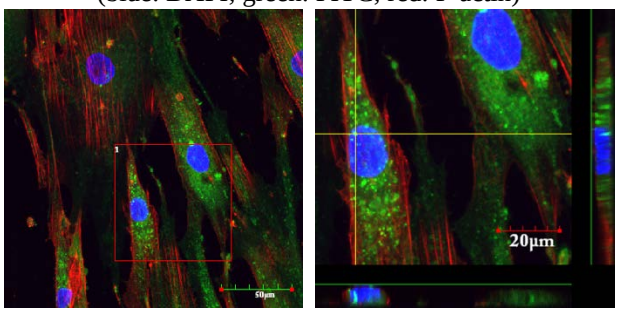
Reperfusion injury of MI heart, which is caused by free radical damage, is an important issue in thrombolytic therapy. CyA inhibits the opening of MPT pore, thereby reduces cell apoptosis. GSH is a peptide with anti-oxidation ability. We developed a multifunctional PLGA-SA nanoparticle (PS NP) with fluorescence, anti-oxidation, and hBMSC-targeting properties for reducing reperfusion injury of MI hearts. FITC-labeled PS NPs with positive charge were fabricated and loaded with CyA. By the layer-by-layer assembly, GSH was coated on the surface of PS NP, followed by HA (H) absorption. Here, BSA was used as a model drug for GSH. Size and zeta potential of PS NP were 251.4 ± 3.2 nm / +24.9 ± 2.1 mV, and 294.7 ± 9.1 nm / -6.7 ± 0.7 mV for PS/BH NP. For hBMSC uptake experiment. Green fluorescence of NP was first observed at 15 min. The percentage of cells exhibiting fluorescence intensity above arbitrary threshold were 19% and 6% for incubation with PS/BH and PLGA, respectively. In addition, the NPs were located in cytoplasm, and the uptake increases with time. Cell viability of hBMSCs incubated with NPs for 72 h was not influenced, indicating the PS/GH NP is biocompatible. The migration and chemotaxis of hBMSC loaded with CyA encapsulated PS/GH NP would not be influenced, and the NP/hBMSC delivery system would be employed in reducing reperfusion injury of MI hearts.

2h cellular uptake of PS/BH NPs
FITC-labeled PS/BH NPs were observed in cytoplasm
(blue: DAPI; green: FITC; red: F-actin)



PC-8

Multitheranostic nanocapsule encapsulated with multiple drugs and Gd-neutron capture therapy facilitated by stem cell-magneto-based targeting for GBM

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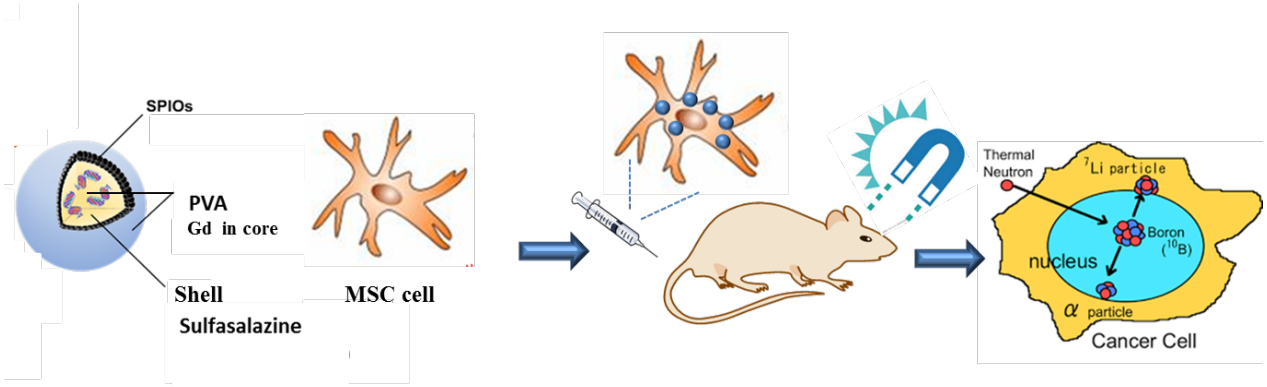
Neutron capture therapy (NCT) had been demonstrated a non-invasive approach for the selective destruction of cancer cells by radiations emitted from nonradioactive NCT agents upon capturing thermal neutrons. In terms of the chemical agents for NCT, ^{6}Lithium, ^{10}Boron, ^{157}Gadolinium, or ^{235}Uranium nuclides have showed the ability for NCT.

Besides the limited delivery of drugs across the blood brain barrier (BBB), no single compound or molecule of NCT agents will be able to target every tumor cell. Therefore, in order to move the NCT therapy to clinical application, it is mandatory to develop the other non-toxic nano-technological and/or cell-based delivery strategies to enhance the biocompatibility and accuracy of NCT for cancer treatment.

Mesenchymal stem cells (MSCs) regarding as a cellular vehicle/vector showed a unique tumor-homing tropism for targeted delivery of anticancer substances to animal models of various tumors, including melanoma, glioblastoma, and breast cancer. Glioblastoma multiforme (GBM), the most common deadly malignancy of the central nervous system. It is crucial to identify the ideal therapeutic protocols to target the tumor tissue while sparing healthy brain.

In this report, we develop a MSC-based vehicles terrace that integrate the tumor homing of stem cells (MSC-PVA@fe-SSZ-Gd) and multifunctionalized core-shell Polyvinyl alcohol-derived nanocapsule strengthened by iron oxide (PVA@fe), which was equipped with interior Gd-DTPA surrounding by outer chemotherapeutic drug(Sulfasalazine). We report the first platform of GBM treatment using stem cell-oriented chaperon delivery of magnet-targeted multimodality fucoidan-derived nanoparticle incorporating with both GD-DTPA and SSZ for triple MR cancer imaging, Gd-NCT radiotherapy and chemotherapy.



Schematic illustration the purpose of the MSC-PVA@fe-SSZ-Gd nanoparticles.

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PC-9

Targeted Delivery of Functionalized Upconversion Nanoparticles for Near-Infrared Triggered Photothermal/Photodynamic Therapies of Orthotopic Glioblastoma

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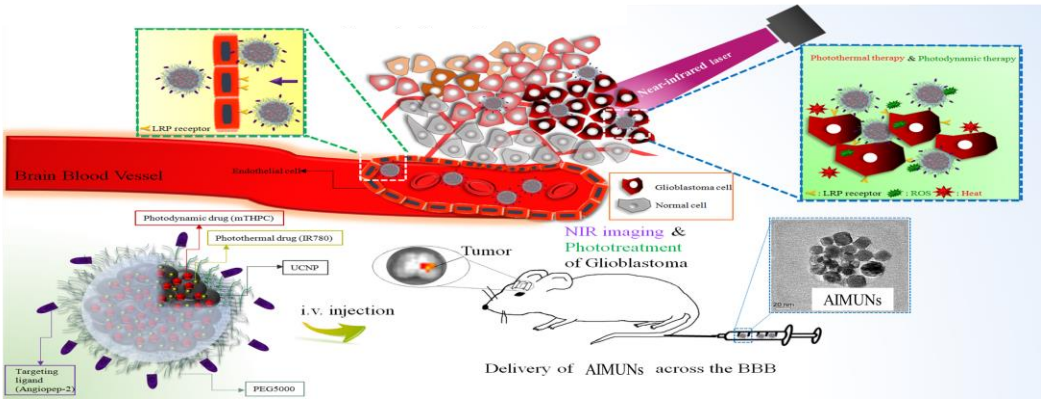
In order to enhance the photodynamic/photothermal therapeutic efficacy on malignant brain tumor, a versatile upconversion nanoparticle drug delivery system capable of converting the deep tissue penetrating near-infrared light into visible wavelength for activating photochemical reaction were developed in this work. The drug-loaded nanoparticles were obtained from the assembly of oleic acid-coated upconversion nanoparticles (UCNPs) along with maleimide-conjugated poly(ethylene glycol)-cholesterol (Mal-PEG-Chol), as a surfactant, and hydrophobic photosensitizers, IR-780 (for photothermal therapy, PTT) and mTHPC (for photodynamic therapy, PDT), in aqueous solution. The therapeutic payload loading of IR-780 and mTHPC was achieved via hydrophobic association. To enhance the nanoparticle accumulation at target sites, the targeting moiety, angiopep-2, capable of specifically binding to the low density lipoprotein receptors of tumor endothelial cells and malignant astrocytes was conjugated at the end of PEG on the NP surfaces. The drug-loaded NPs with a ca. 80 nm in diameter exhibit an excellent colloidal stability in physiological conditions. The drug loading contents are 5.9 wt% for IR-780 and 8.1 wt% for mTHPC. *In vitro* data demonstrate a successful selective accumulation of drug-loaded NPs in ALTS1C1 cells (murine astrocytoma cells) and pronounced cytotoxicity elicited by combinational therapies of PDT and PTT. *In vivo* results show the promising accumulation of therapeutic NPs at brain tumor and therapeutic effect after the dual-modality treatment. This work demonstrates great potential of UCNP-mediated PDT and PTT in brain cancer therapy.



Schematic illustration of angiopep-2 decorated IR780/mTHPC-loaded upconversion nanoparticles (AIMUNs) as a theranostic platform for brain tumor treatment.

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PC-10

Biodegradable in situ Gelling Polymers for the Treatment Dye Eye Disease

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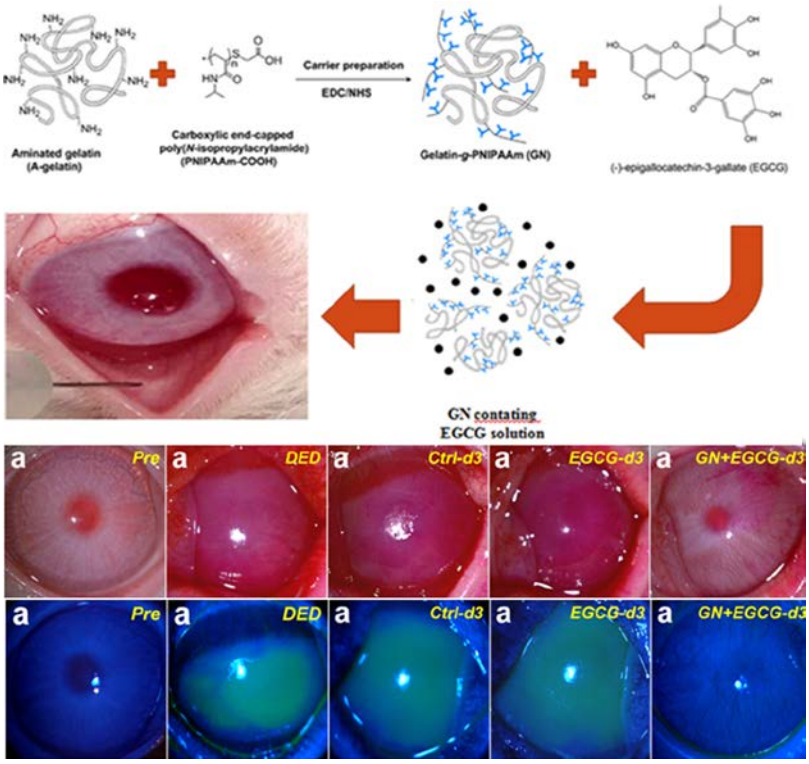
The purpose of this study is to develop gelatin-*g*-poly(*N*-isopropylacrylamide) (GN)-based ophthalmic drug carriers. We investigate the feasibility of using biodegradable in situ gels as topical ocular slow-release system. The epigallocatechin gallate (EGCG) is delivered by GN copolymers to treat external ocular disorders such as dry eye diseases. Approximately 85% of weight loss of GN is noted in the presence of 1000 ng/ml matrix metalloproteinase-9 (MMP-9) during 3 days of in vitro degradation. The drug loading capacity is approximately 68.57 %. Results of in vitro drug release studies demonstrate a sustained slow-release pattern of EGCG by using GN carrier materials. In addition, the drug concentration in the release buffer can effectively inhibit the MMP-9 action associated with dry eye diseases. After establishment of a dry eye animal model by topically instilled benzalkonium chloride solution, the biodegradable in situ GN containing EGCG is delivered to the conjunctival sac. Results of slit-lamp biomicroscopy, rose bengal staining, Schirmer's tear test, and corneal tissue H&E stain show that ocular delivery of EGCG using GN carriers can enhance drug bioavailability.



PC-11

Development of Drug-Eluting Intraocular Lens Improves Post-Cataract Surgical Complications

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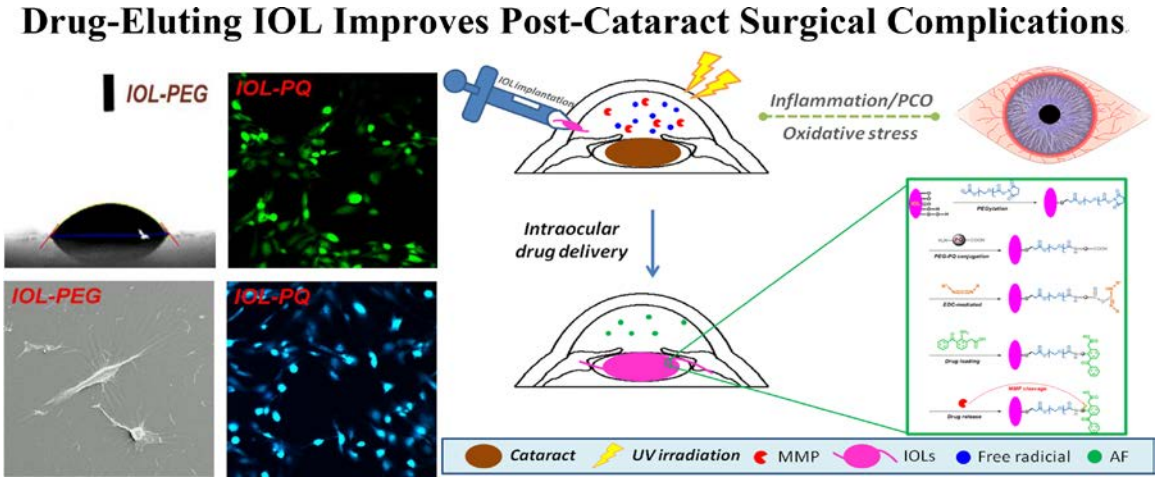
The crystalline lens is a transparent, biconvex structure in the eye that participates in light refraction. Cataract is a serious and common eye condition affecting more than 20 million worldwide. To improve the cataract surgery-related postoperative inflammation and posterior capsule opacification, a drug-eluting intraocular lens (IOL) is developed in this study to extend the duration of drug action and to increase the ocular bioavailability. After the treatment by plasma chemistry, the IOL samples are further modified with heterobifunctional poly(ethylene glycol) (PEG) derivatives and matrix metalloproteinase (MMP)-sensitive peptide. The amfenac that inhibits cyclooxygenase type-2 (COX-2) is further covalently bound to the IOL. After specific cleavage of MMP-sensitive peptide sequence in simulated physiological buffer, the drugs can be released from the carriers in a sustained manner. Our findings suggest that the drug-eluting IOLs can significantly alleviate the inflammation reaction due to IOL implantation.



PC-12

Dual Stimuli-Responsive Chemodrug/Magnetite-Loaded Solid Lipid Nanoparticles for Enhanced Intracellular Drug Delivery and Effective Chemo-Thermal Therapy

Te-I Liu,[1] Ting-Yu Lu,[1] Hsin-Hung Chen,[2] Wen-Chia Huang[1] and Hsin-Cheng Chiu[1*]
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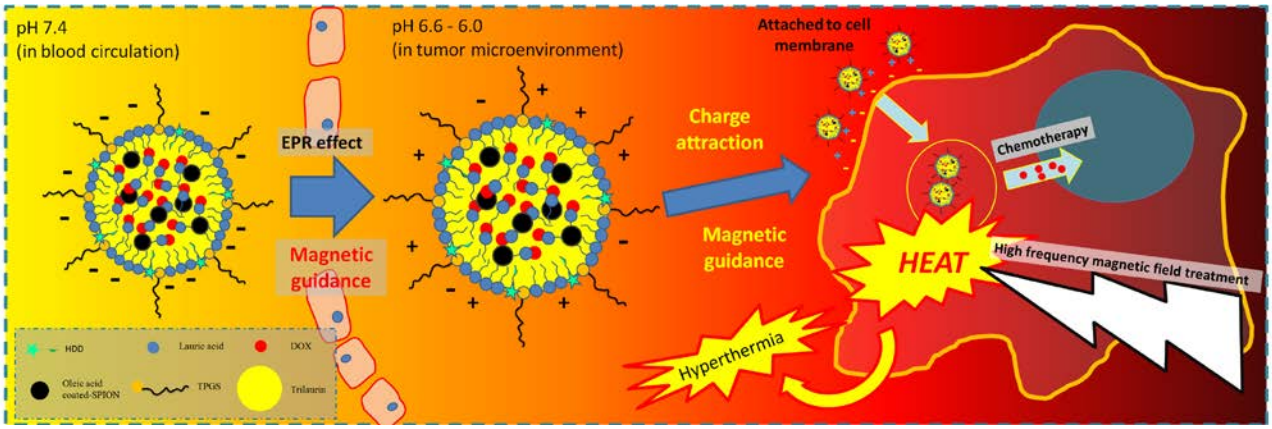
In this work, a versatile chemodrug/magnetite delivery system based on the solid lipid nanoparticles (SLNs) as nanovehicles capable of enhancing intracellular therapeutic accumulation via electrostatic association and magnetic guidance for effective chemo-thermal therapy against cancer cells was developed. To endow the SLNs with pH-inducible surface charge transition, a pH-responsive lipid derivative was first synthesized via the covalent conjugation of histamine with 1-dodecanal prior to SLN preparation. In addition, the positively charged anticancer drug, doxorubicin (DOX), was complexed with the negatively charged lipids via electrostatic interaction. Through the hydrophobic association of the drug/lipid complexes with glycerol trilaurate, magnetite nanoparticles and cholesterol-conjugated poly(ethylene glycol) in aqueous solution, the drug/magnetite-loaded SLNs with a particle size of ca 120 nm in diameter were obtained. The SLNs exhibit excellent colloidal stability and drug loading efficiency (88%) and its confinement. With external medium pH being adjusted to acidic pH of tumor microenvironment (pH 6.6 ~ 6.0), a dramatic surface charge transition (-6 to +4 mV) of the SLNs was observed due to the extensive protonation of histamine groups. The DOX liberation can also thus be triggered by the disruption of lipid/DOX ionic complexes under acidic conditions. *In vitro* data demonstrate that the cellular uptake of SLNs by cancer cells was largely enhanced through electrostatic association between positively charged SLNs and negatively charged cell walls in culture medium at pH 6.5 under magnetic field guidance. Owing to the pronounced intracellular accumulation, the SLNs show the superior chemotherapy and hyperthermia effect against cancer cells under alternative magnetic field treatment, demonstrating a great potential of chemo-thermal treatment in cancer therapy.



Schematic illustration of the dual stimuli-responsive chemodrug/magnetite-loaded SLNs for enhanced intracellular drug delivery and effective chemo-thermal therapy against cancer cells.

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PC-13

Dual-functional nanoparticles targeting CXCR4 and delivering anti-angiogenic siRNA ameliorate liver fibrosis

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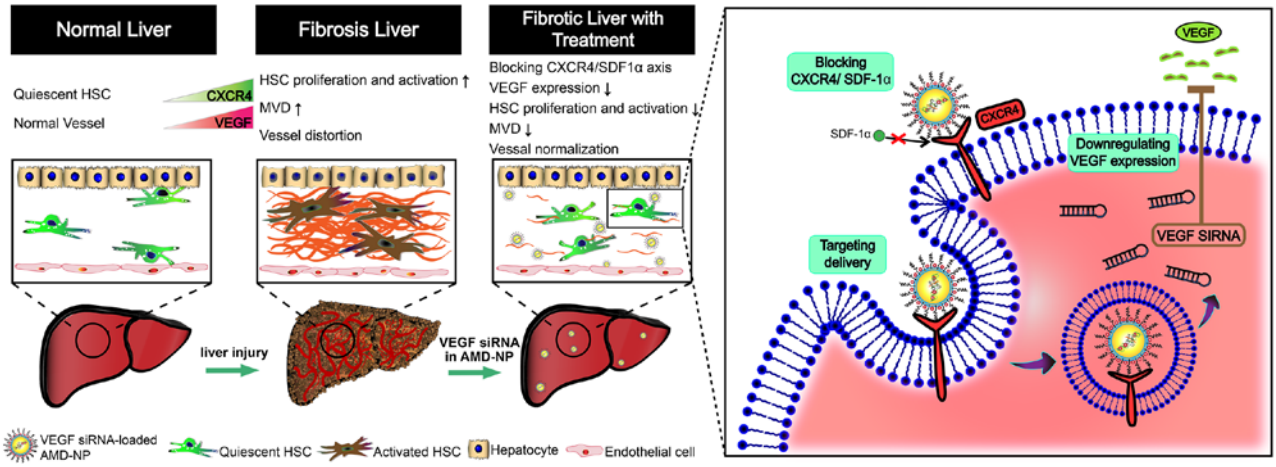
The progression of liver fibrosis, an intrinsic response to chronic liver injury, is associated with hepatic hypoxia, angiogenesis, abnormal inflammation, and significant matrix deposition, leading to the development of cirrhosis and hepatocellular carcinoma (HCC). Due to the complex pathogenesis of liver fibrosis, anti-fibrotic drug development has faced the challenge of efficiently and specifically targeting multiple pathogenic mechanisms. Therefore, we developed a CXCR4-targeted nanoparticle (NP) to deliver VEGF siRNA as an anti-angiogenic substance into fibrotic livers. AMD3100, a CXCR4 antagonist that was incorporated into the NPs, served dual functions: it acted as a targeting moiety and suppressed the progression of fibrosis by inhibiting the proliferation and activation of hepatic stellate cells (HSCs). We demonstrated that CXCR4-targeted NPs can efficiently deliver VEGF siRNAs into fibrotic livers, decrease VEGF expression, suppress angiogenesis and normalize the distorted vessels in the fibrotic livers of CCl4-treated mice. Furthermore, blocking SDF-1α/CXCR4 by CXCR4-targeted NPs in combination with VEGF siRNA significantly prevented the progression of liver fibrosis in CCl4-treated mice. In conclusion, CXCR4-targeted multifunctional NPs that co-deliver VEGF siRNAs and AMD3100 provide an effective anti-fibrotic therapeutic strategy.



The inhibition of the SDF-1α/CXCR4 axis and VEGF expression in the fibrotic livers achieved by a single formulation synergistically suppressed the progression of liver fibrosis in the CCl_4-induced mouse model of liver fibrosis.

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PC-14

Microporous Coating Tablet as Oral Drug Delivery System with Constant Release

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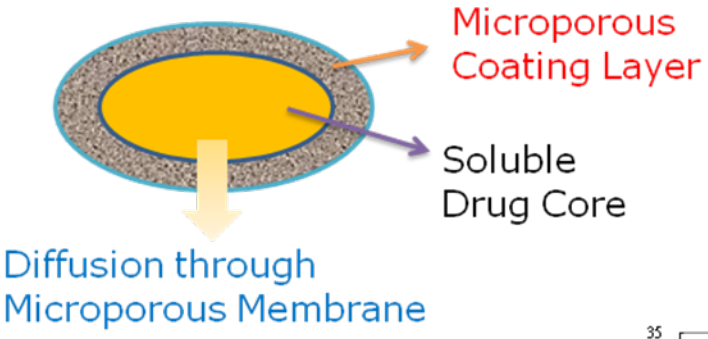
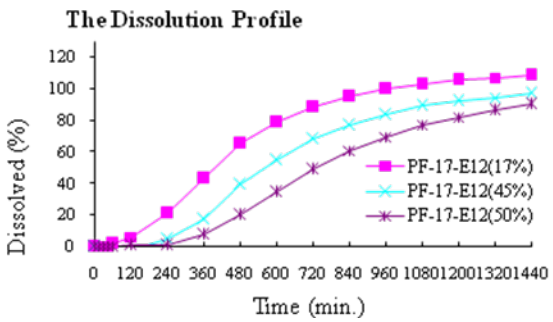
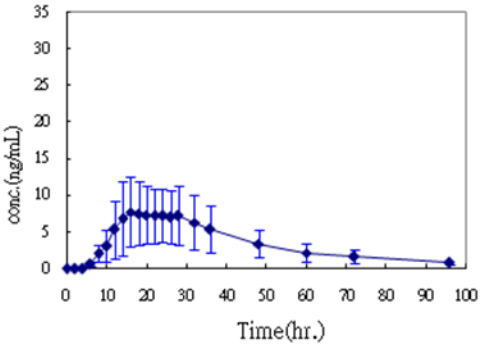
The OROS delivery system can be applied for once-daily administration. Its pharmacokinetic profile results in a more stable serum concentration (1). In this study, we used the model drug(PF-17) and tried to use Eudragit NE 30D as coating material, and made the microporous film with addition of mannitol in coating formulation. By this way, we can prepare the controlled release tablet with constant rate without using laser drilling. We compare the different formulations in tablet coating. The results show the ratio of soluble molecules in coating material will modify the dissolution profile of drug from tablets. However, the drug dissolution profile in pH 6.8 did not depend on the ratio of soluble material. This may result from the low solubility of drug in neutral pH condition. From these result, the microporous membrane for controlled release will depend on the condition of drug for diffusion. PF-17 have high solubility in acidic condition, and follow the diffusion through these porous coating. Furthermore, the soluble material in coating membrane is less than 40%, and membrane will be changed completely. We chose the coating formulation containing 45% soluble materials to study the effect of coating thickness. The increasing thickness of coating materials will delay the onset time of drug in dissolution profile. The coating tablets were applied in health volunteers and the pharmacokinetic profiles showed the sustained release effect *in vivo*. The result demonstrated the membrane controlled release delivery system is another option to prepare the extended-release tablet for constant rate.







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PC-15

Synergistic Combination Therapy Using a Core-Shell Lipid-Based Nanocapsule with Tunable Shell Thickness

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Combination therapy has great potential to demonstrate synergistic therapeutic effect toward diseased cells, and even can overcome the multi-drug resistance (MDR) through various mechanisms of action. However, encapsulating drugs with different physicochemical properties into a common vehicle is challenging, especially when it comes to hydrophobic and hydrophilic compounds. On the basis of double emulsion approach, a core-shell lipid-based nanocapsule (CSLNs) was developed to simultaneously encapsulate a hydrophobic anticancer drug, paclitaxel (PTX), in the shell and a hydrophilic anticancer drug, doxorubicin (DOX), in the core. Moreover, the combination of drugs in different ratios has been evaluated for searching the optimal synergistic effect in MCF-7/ADR breast cancer cells with MDR. In addition, manipulation of the shell thickness of CSLNs was found to adjust drug release rate and the further thickness- and time-dependent cytotoxicity is under investigation. The CSLNs have potential as being a feasible nano-platform for combination anticancer therapy.

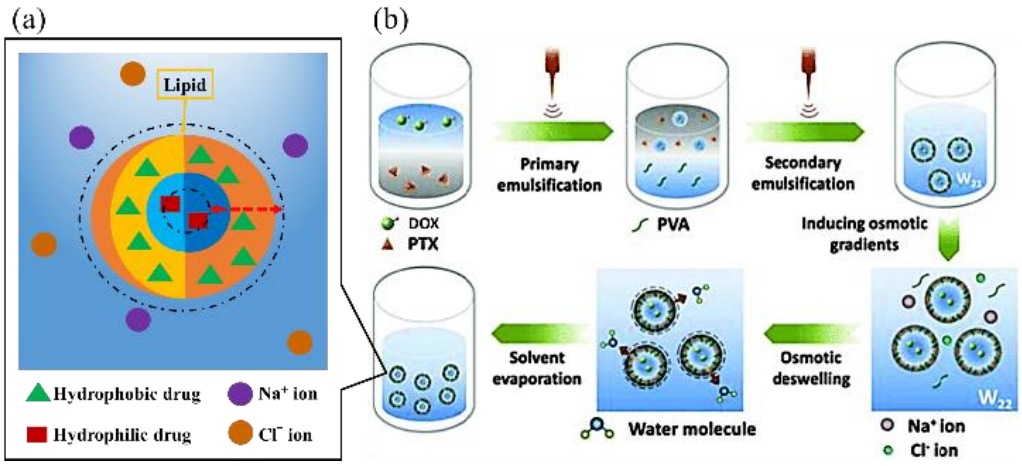

Figure 1. (a) Illustration of CSLNs loaded with a hydrophobic drug in the shell and a hydrophilic drug in the core. Variation of shell thickness is represented. (b) Scheme of the CSLNs fabrication process.

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PC-16

Preparation and Evaluation of Chrysin Loaded Polyketal Nanoparticles

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Chrysin, a kind of flavonoid, has been evaluated as a natural chemopreventive agent due to its antioxidative[1] and anti-inflammatory[2] properties. However, the bioavailability of chrysin has been limited because of poor aqueous dispersibility and extremely low solubility. Given these limitations with current chrysin delivery method, a new delivery system which can increase the aqueous dispersibility and bioavailability of chrysin is needed. Polyketals, a family of biodegradable polymers, have been used as drug delivery vehicles for treating inflammatory diseases because they have excellent biocompatibility and do not generate inflammatory acid degradation products as do polyester-based biomaterials. Chrysin-loaded polyketal microparticles (Chrysin-PKNs) were developed to improve the aqueous dispersibility of chrysin. The encapsulation efficiency of Chrysin-PKNs ranges from 68.9 to 84.9 % depends on the preparation methods. More importantly, Chrysin-PKNs showed great aqueous dispersibility and sustained release properties. We expected this system will enhance the bioavailability of Chrysin.

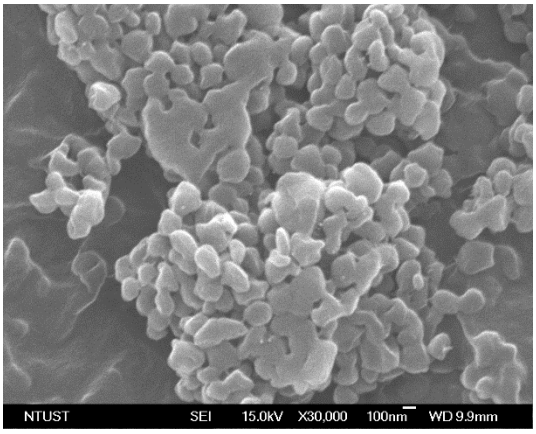

Figure: SEM image of Chrysin-PKNs

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PC-17

Fabrication of Gelatin Covered Mesoporous Silica Nanoparticles as Sustained Release Drug Delivery System for Glaucoma Treatment

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Glaucoma has become a worldwide optic neuropathy with high chance to induce irreversible ocular injury. Intraocular pressure (IOP) is the only manageable symptom in primary open-angle glaucoma. The concept of this work is shown in Fig. 1. We fabricated gelatin covered mesoporous silica nanoparticles (GM) as carrier to deliver pilocarpine via intracameral administration. The *in vitro* release profile showed that GM0.05 had high release percentage (50%) and long-lasting release profile (36 days). The *in vivo* animal studies showed that GM0.05 could maintained IOP on eyes with ocular hypertension for 21 days. Other *in vivo* results indicated that GM had high biocompatibility and bioavailability. We proposed that the change of microenvironment caused from degradation of gelatin by matrix metallprotease-2 would induce the release of drug from carrier.

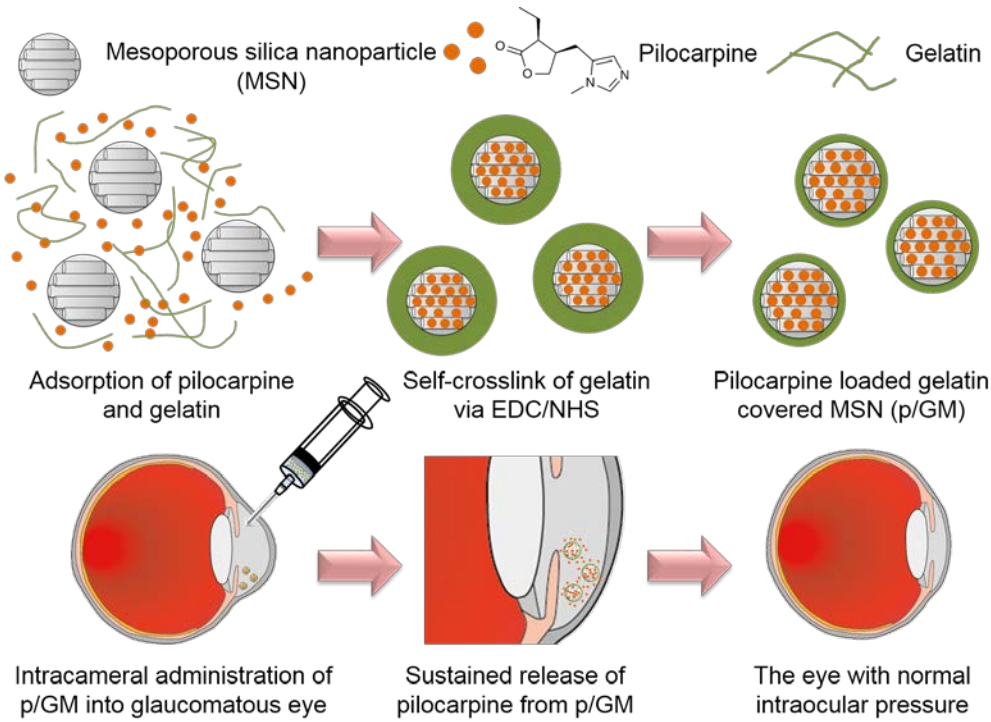

Figure 1. Synthesis of pilocarpine loaded gelatin covered MSN as an ocular drug delivery system to reduce intraocular pressure by intracameral administration into anterior chamber.

PC-18

Synthesis of inorganic nanoparticles/organic alginate composite for guiding chemotherapy of bladder cancer

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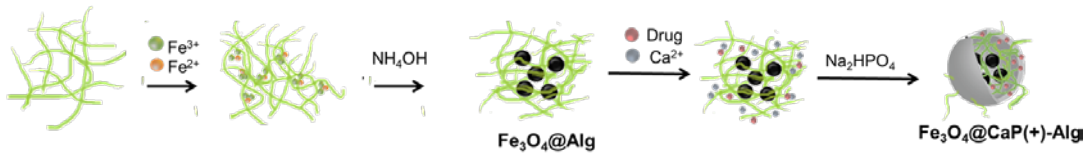
We successfully synthesized Fe_3O_4@CaP-Alg nanocomposite with inorganic nanoparticles /organic alginate polymer, including Fe_3O_4 with superparamagnetic property and the pH-responsive CaP shell which can encapsulate an antitumor drug, doxorubicin with an encapsulation efficiency of about 80%. We then functionalize the nanocomposite with c(RGDfK) peptide for targeting bladder cancer cell line (i.e. T24). The relative cell viabilities decrease to 0.1-0.3, depending on the concentration of Fe_3O_4@CaP(+)-Alg-RGD. The nanocomposite can be guided by magnetism to specific location that can increase the local concentration of material and result in better inhibition of the cancer cell with the lowest impact on adjacent cell.



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PC-19

Encapsulation of low dosage propranolol by DSPC liposomes improved bone microarchitecture in ovariectomized rats

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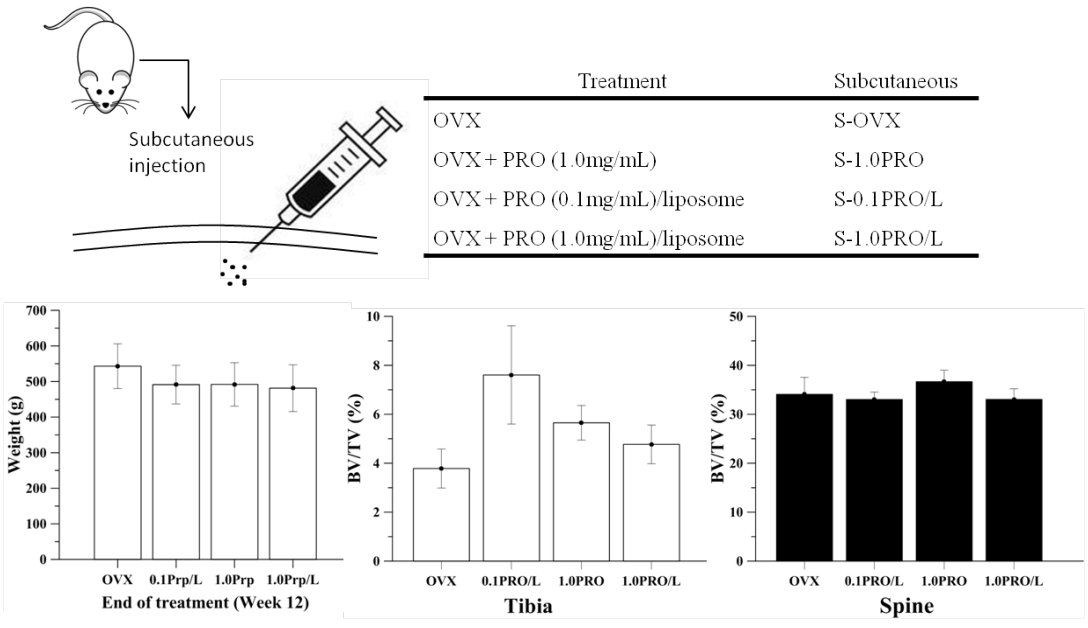
Propranolol (PRP), a type of beta blocker which often used to treat heart disease, has recently been discovered to have therapeutic effects against bone loss. In our previous study, the stimulatory effects of liposomal PRP on the proliferation and differentiation of human osteoblastic cells *in vitro* suggested that the prepared liposomes-encapsulated PRP may have anabolic effects on bone *in vivo*. The present study further investigate the effects of PRP on bone formation in ovariectomized (OVX) rats. Rats subjected to OVX were administered with PRP for 12 weeks via subcutaneous (s.c.) injection. No obvious changes on rat body weight were observed. Changes in microarchitecture of both proximal tibia and the fourth lumbar spine were assessed and compared between PRP-treated and non-treated groups using micro-computed tomography. The ratio of bone volume over total volume (BV/TV) was evaluated. Our preliminary results showed that PRP treatment increased BV/TV insignificantly in tibia whereas no changes of BV/TV in the forth lumbar spine, as compared to non-treated group. Liposomal PRP at lower dosage (0.1 mg/mL) improve BV/TV (from 3.8 % to 7.6 %) on tibia, which was higher than at high encapsulation dosage (1.0 mg/mL, BV/TV 4.8 %). Improvement on liposomal formulation or drug delivery routes would be required to display more obvious effects on bone formation for PRP. In conclusion, low dosage of PRP encapsulated in liposomes are potentially capable of recovering the bone microarchitecture in OVX rats.



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PC-20

ZnO-loaded Pluronic Nano-micelles for Tumor-targeting Drug Delivery System

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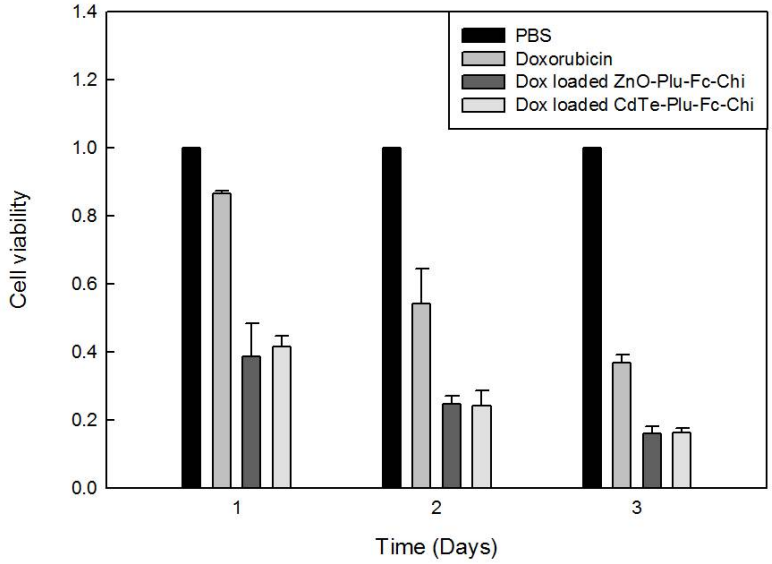
In this study, ZnO quantum dots (QDs) were firstly synthesized by a chemical hydrolysis method. Folic acid was conjugated with chitosan to synthesis the biofunctional chitosan (Fc-Chi). Then, the QDs and Doxorubicin (Dox) were encapsulated with Pluronic nano-micelles. Finally, the surface of Pluronic micelles containing QDs was modified by folate-conjugated chitosan to obtain tumor-targeting drug delivery carrier Dox loaded QDs-Plu-Fc-Chi nano micelles. ZnO QDs have spherical shape with particle size of 4.3 nm. Photoluminescence (PL) analysis indicates ZnO QD has characteristics of blue shift and its emission wavelength is 365 nm. These observations reveal that QDs particles have quantum size and they can be used for in vivo imaging analysis. Nano micelles modified with different concentration of chitosan have spherical shape with particle size ranging from 87-154 nm. FTIR analysis reveals that nano-micelles were successfully prepared from pluronic and chitosan. X-ray analyses confirm that QDs and Doxorubicin are actually encapsulated with the micelles and have very good loading stability. The micelles are positive charge and they can be effectively adhered to the negatively charged of the cellular membrane. Confocal microscope observation and fluorescence analysis demonstrate that QDs and Doxorubicin have fluorescence intensity after encapsulation inside the micelles. The micelles which modified by folate-conjugated chitosan have controlled drug release behavior. And finally, the MTT assay reveals that Dox loaded QDs-Plu-Fc-Chi can be used in cancer therapy.



MTT assay of Dox loaded Pluronic nano-micelles incorporating ZnO and CdTe quantum dots, respectively.

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PC-21

A Nanoformulation of Antimicrobial Peptides and Anticancer Drugs in PEGylated Liposomes Inhibits Multidrug Resistance in Different Cancer Cells

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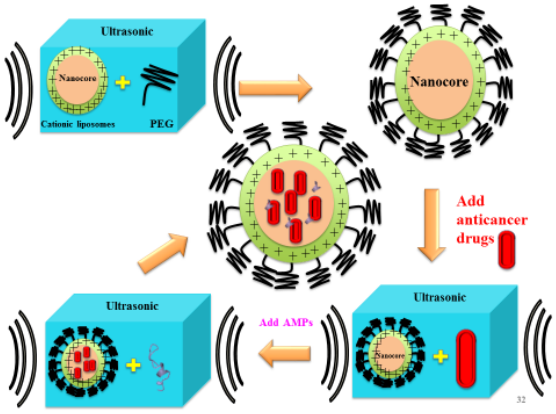
Antimicrobial peptides (AMPs) possess different structure and mechanism(s) in comparison with traditional multidrug resistance (MDR) inhibitors. For the purpose of reducing off-target normal cell toxicity, it is rational to incorporate various AMPs and anticancer drugs in PEGylated liposomes. In the present study, we report multifunctional liposomes encapsulating epirubicin and different AMPs to circumvent MDR in various human cancer cells. Co-treatment of cancer cells with PEGylated liposomal formulation of epirubicin and AMP gave rise to a significant increase in the cytotoxicity of epirubicin. The liposomal formulations of epirubicin and/or AMP were found to noticeably increase the intracellular levels of reactive oxygen species in cancer cells. Moreover, these treatments were demonstrated to considerably reduce mRNA expression levels of MDR transporters. The addition of AMP in liposomes was shown to markedly enhance the epirubicin uptake into cancer cells. In addition, the PEGylated liposomes of epirubicin and AMP were also found to trigger apoptosis in cancer cells. The apoptosis induction was also confirmed by the rise in apoptosis phase of cell cycle. Altogether, our results provide the supporting evidence that co-incubation with PEGylated liposomes of AMP and epirubicin caused programmed cell death in different human cancer cells through modulation of multiple signaling pathways. Thus, AMPs may be developed as a new generation of MDR-reversing adjuvant to potentiate the efficacy of cancer chemotherapeutics.



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