附件 3：

内蒙古自治区重点实验室 20 18年度工作报告

实验室名称：	**内蒙古自治区蒙药化学重点实验**
实验室主任：	**博格日勒图**
主管部门：	**内蒙古大学**
依托单位名称：	**化学化工学院**
通讯地址：	**呼和浩特市大学西路 235 号**
邮政编码：	**010021**
联系人：	**韩淑琴**
联系电话：	**0471-4991090**
E-mail 地址：	**chem-hshq@imu.edu.cn**

2019 年 1 月 2 日 填报

2018 年制

一、基本信息

实验室名称	中文：内蒙古自治区蒙药化学重点实验室			
	英文：Inner Mongolia key Laboratory of Mongolian Medicine Chemistry			
研究方向（据实增删）	研究方向 1	蒙药化学		
	研究方向 2	化学生物学		
	研究方向 3	药用植物化学		
实验室主任	姓名	博格日勒图	出生年月	1957.12
	职称	教授	专业领域	药物化学
	任职时间	2003 年	在依托单位职务	无
学术委员会主任	姓名	哈达	出生年月	1977.11
	职称	教授	专业领域	细胞生物学
	任职时间	2017 年	所在单位及职务	内蒙古大学生命科学学院

二、重点实验室年度情况

实验室经费（合计：万元）	经费构成	运行费（万元）	科研经费（万元）	仪器设备购置费（万元）	人员费（万元）
	国家	0	42	0	0
	部门（地方）	0	58	142	0
	依托单位	0	0	0	0
	合计	0	100	142	0

科研条件（当前情况）	实验室面积	380 平方米	
	科研仪器、设备累计	152 台（套）	689 万元（原值）
	大型仪器、设备（50 万元以上）累计	3 台（套）	386 万元（原值）

科研情况	项目（课题）	3 项	经费合计	100 万元
	承担国家级项目（课题）	1 项	经费合计	42 万元
	承担省部级项目（课题）	2 项	经费合计	58 万元

	承担地市级项目（课题）		0 项	经费合计		0 万元
	承担横向项目（课题）		0 项	经费合计		0 万元
人才队伍	固定人员		8 人			
	高级职称	5 人	中级职称	3 人	初级职称	0 人
	流动人员		0 人			
	高级职称	0 人	中级职称	0 人	初级职称	0 人
	院士		固定	0 人	千人计划	固定 0 人
			流动	0 人		流动 0 人
	万人计划		固定	0 人	青年千人	固定 0 人
			流动	0 人		流动 0 人
	百千万人才		固定	0 人	杰青或优青	固定 0 人
			流动	0 人		流动 0 人
	省部级人才计划		固定	2 人		
			流动	0 人		
运行管理	管理制度		1 项	是否全部实施		是■否□
	组建学术委员会		是■否□	召开会议次数		1 次
开放共享	开放课题		2 项	经费合计		10 万元
	仪器设施对外开放机时		80 小时	开展科普活动		2 次

三、成果统计

获奖情况	国家级奖励	一等奖	0 项		二等奖		0 项
	省、部级科技奖励	一等奖	0 项	二等奖	0 项	三等奖	0 项
	行业科技奖励	一等奖	0 项	二等奖	0 项	三等奖	0 项
论文专著	发表论文	共计	3 篇	SCI	3 篇	EI	0 篇
	专著	国内出版	0 部		国外出版		0 部
知识产权	发明专利	国际	0 项		国内		0 项
	其它专利	国际	0 项		国内		0 项

	标准规范	国际标准	0 个	国家标准	0 个
		行业标准	0 个	团体标准	0 个
产学研合作	与高校、院所合作	0 项	合作经费	0 万元	
	与企业合作	0 项	合作经费	0 万元	
行业支撑	成果转移转化	0 项	转移转化收入	0 万元	
	行业技术服务	0 项	服务收入	0 万元	

注：以上各表中所有数据指截止到统计年度所得数据或统计年度当年情况，项目经费指每个项目的总经费。

四、实验室本年度建设情况

简要介绍实验室本年度研发条件与能力、科研水平与贡献、团队建设与人才培养、开放交流与运行管理等情况。

本年度研发条件与能力：本年度国家自然科学基金项目在研一项，自治区自然科学基金在研一项；发表 SCI 收录论文 3 篇，期中一篇是常用蒙药-额尔敦乌日勒的作用机理研究成果，突破了传统蒙医药领域 SCI 论文零的记录；培养硕士博士生：本年度 1 名博士生毕业，在学 8 名，4 名硕士研究生毕业，在学 10 名。

我们积极进展学术交流、国际合作、社会开放，对国内外来实验室进行学术活动的合作者可提供实验设施等科研条件；博格日勒图教授到基层向农牧民进行健康知识科普讲座，以及到地方中小学，进行科学应用发展方面的课外知识讲座。

重点实验室实行实验室主任负责制，制定有详细的实验室规章制度；下设两名专职人员具体负责实验室的日常管理、仪器设备的使用维护、研究生的管理等各项工作；学术委员会定期进行学术交流活动。

五、审核意见

实验室承诺所填内容属实，数据准确可靠。 实验室主任： （单位公章） 年　月　日
依托单位审核意见 依托单位负责人签字： （单位公章） 年　月　日
主管部门审核意见 主管部门负责人签字: （单位公章） 年　月　日

附件

项目批准号	81560568
申请代码	H3002
归口管理部门	
依托单位代码	01002108A1582-1273

81560568100438O

国家自然科学基金委员会

资助项目计划书

资助类别：地区科学基金项目

亚类说明：

附注说明：

项目名称：降血脂活性天然产物苹菱宁特异性靶标的确定及其作用机理研究

直接费用：35万元　　间接费用：7万元

项目资金：42万元　　执行年限：2016.01-2019.12

负 责 人：胡日查

通讯地址：内蒙古自治区呼和浩特市大学西路235号

邮政编码：010021　　电　　话：0471-4993165

电子邮件：hbaigude@imu.edu.cn

依托单位：内蒙古大学

联 系 人：刘志亮　　电　　话：0471-4995414

填表日期：2015年09月06日

国家自然科学基金委员会制

Version：1.004.380

内蒙古自治区
科技创新引导项目计划任务书

项 目 编 号：

项 目 名 称：创新蒙药“胡芪降脂胶囊”的
长期毒性实验研究

项 目 负 责 人：博·格日勒图

项 目 组 织 单 位：内蒙古自治区财政厅

项 目 承 担 单 位：内蒙古大学

联 系 电 话：0471-4992257

资 助 金 额：50 万元

填 报 日 期：2016 年 4 月 27 日

内蒙古自治区财政厅制

内蒙古自治区自然科学基金项目
批 准 意 见 表

申 请 者	昭日格图	项目编号	2016MS0812
项目名称	蒙药苹发在效成分苹发宁的结构与体内药效及药代动力学研究		
工作单位	内蒙古大学		
资助金额	8.0 万元	起止年限	2016-2018
通讯评审专家意见：			

polymers

MDPI

Article

Sugar Functionalized Synergistic Dendrimers for Biocompatible Delivery of Nucleic Acid Therapeutics

Shuqin Han [1], Tsogzolmaa Ganbold [1], Qingming Bao [1], Takashi Yoshida [2] and Huricha Baigude [1,*]

[1] School of Chemistry & Chemical Engineering, Inner Mongolia Key Laboratory of Mongolian Medicinal Chemistry, Inner Mongolia University, 235 West College Road, Hohhot 010021, China; chem-hshq@imu.edu.cn (S.H.); tsogi001@mail.imu.edu.cn (T.G.); qingming@mail.imu.edu.cn (Q.B.)

[2] Department of Bio and Environmental Chemistry, Kitami Institute of Technology, 165 Koen-cho, Kitami, Hokkaido 090-8507, Japan; yoshida@chem.kitami-it.ac.jp

* Correspondence: hbaigude@imu.edu.cn; Tel.: +86-471-499-3165

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Abstract: Sugars containing cationic polymers are potential carriers for in vitro and in vivo nucleic acid delivery. Monosaccharides such as glucose and galactose have been chemically conjugated to various materials of synergistic poly-lysine dendrimer systems for efficient and biocompatible delivery of short interfering RNA (siRNA). The synergistic dendrimers, which contain lipid conjugated glucose terminalized lysine dendrimers, have significantly lower adverse impact on cells while maintaining efficient cellular entry. Moreover, the synergistic dendrimers complexed to siRNA induced RNA interference (RNAi) in the cells and profoundly knocked down green fluorescence protein (GFP) as well as the endogenously expressing disease related gene Plk1. The new synergic dendrimers may be promising system for biocompatible and efficient siRNA delivery.

Keywords: sugar functionalization; synergistic dendrimer; siRNA delivery; green fluorescence protein; Plk1

1. Introduction

Inhibiting the expression of disease related genes at the messenger RNA (mRNA) level has great potential for clinical applications. By the precise design of single or double stranded short nucleic acids sequences, any existing primary or mature RNA transcripts in the cells can be targeted and subsequently hydrolyzed, which is a dramatically advanced drug design compared to the traditional small molecule based drug screen that can only target up to 5% of the total proteins in the cell [1]. There are two related but distinct approaches to target mRNA: the antisense oligonucleotides (ASOs) based approach and the short interfering RNA (siRNA) based approach. While four ASOs (i.e., fomivirsen [2], mipomersen [3], eteplirsen [4], and nusinersen [5]) have been in clinical applications for treatment of diseases, no siRNA therapeutics have been approved by FDA so far [6], although the efficiency of siRNA is significantly higher than any unmodified or chemically modified ASO. Thanks to the highly efficient RNA-induced silencing complex (RISC) [7], siRNA targets and degrades specific mRNA highly efficiently, while single stranded ASOs bind the complementary sequence site of the target mRNA through Watson–Crick base pairing and inactivate it [8]. While chemically stabilized ASOs can be delivered to the cells without carriers, the double stranded siRNAs usually need carriers for protection from nuclease attack, efficient delivery to the cells, and avoiding immune responses, among other reasons. Failed clinical trials for chemically conjugated naked siRNAs such as cholesterol-conjugated siRNA and siRNA-GalNac [9] suggested that the lack of an efficient biocompatible delivery system is one of the bottlenecks for the development of RNA interference (RNAi) therapeutics.

ACS APPLIED MATERIALS & INTERFACES

Research Article

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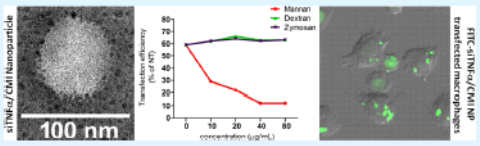
www.acsami.org

Design of Mannose-Functionalized Curdlan Nanoparticles for Macrophage-Targeted siRNA Delivery

Tsogzolmaa Ganbold and Huricha Baigude*

School of Chemistry & Chemical Engineering, Inner Mongolia Key Laboratory of Mongolian Medicinal Chemistry, Inner Mongolia University, 235 West College Road, Hohhot, Inner Mongolia 010020, P. R. China

ABSTRACT: 6-Amino-6-deoxy-curdlan is a promising nucleic acid carrier that efficiently delivers plasmid DNA as well as short interfering RNA (siRNA) to various cell lines. The highly reactive C6-NH_2 groups of 6-amino-6-deoxy-curdlan prompt conjugation of various side groups including tissue-targeting ligands to enhance cell-type-specific nucleic acid delivery to specific cell lines. Herein, to test the primary-cell-targeting efficiency of the curdlan derivative, we chemically conjugated a macrophage-targeting ligand, mannose, to 6-amino-6-deoxy-curdlan. The resulting curdlan derivative (denoted CMI) readily complexed with siRNA and formed nanoparticles with a diameter of 50−80 nm. The CMI nanoparticles successfully delivered a dye-labeled siRNA to mouse peritoneal macrophages. The delivery efficiency was blocked by mannan, a natural ligand for a macrophage surface mannose receptor (CD206), but not by zymosan, a ligand for the dectin-1 receptor, which is also present on the surface of macrophages. Moreover, CMI nanoparticles were internalized by macrophages only at 37 °C, suggesting that the cellular uptake of CMI nanoparticles was energy-dependent. Furthermore, CMI nanoparticle efficiently delivered siRNA against tumor necrosis factor α (TNFα) to lipopolysaccharide-stimulated primary mouse peritoneal macrophages. In vivo experiments demonstrated that CMI nanoparticles successfully delivered siTNFα to mouse peritoneal macrophages, liver, and lung and induced significant knockdown of the TNFα expression at both messenger RNA and protein levels. Therefore, our design of CMI may be a promising siRNA carrier for targeting CD206-expressing primary cells such as macrophage and dendritic cells.



KEYWORDS: *curdlan, short interfering RNA, macrophage, mannose receptor, TNFα*

INTRODUCTION

RNA interference (RNAi) is a promising therapeutic approach that allows post-transcriptional down-regulation of gene expression by designed sequences of double-stranded short interfering RNA (siRNA).[1] Endogenously generated or exogenously introduced siRNA loads to RNA-induced silencing complex and clips target messenger RNA (mRNA) at a specific site, resulting in the expedited turnover of a disease-causing problematic protein.[2] SiRNA can be designed to target any mRNA at very low doses with a sustainable time period, making RNAi technology extremely valuable for curing diseases triggered by nondruggable gene products.[3] However, because of the vulnerable nature of siRNA such as its high susceptibility to nuclease and other environmental elements, protection of siRNA through formulation is usually necessary prior to any type of siRNA delivery (except for highly chemically modified siRNA sequences).[4,5] Naturally occurring macromolecules, with or without chemical modifications, have been extensively investigated for potential applications for in vitro and in vivo siRNA delivery.[6,7]

Wild-type curdlan (β-1,3-D-glucan) has shown the ability of protecting and delivering siRNA.[8,9] With a series of formulations involving several types of macromolecules such as polyethylenimine (PEI) and tRNA, a siRNA delivery microparticle termed GeRP was created. When orally administered, GeRP efficiently delivered siRNA to macrophages residing in several organs including liver, spleen, and lung and induced RNAi against tumor necrosis factor α (TNFα).[10] We synthesized 6-azido-6-deoxy-curdlan for the first time using triphenylphosphine, carbon tetrabromide, and sodium azide. A subsequent reduction of 6-azido-6-deoxy-curdlan by $NaBH_4$ gave 6-amino-6-deoxy-curdlan (denoted 6AC-100), which showed excellent water solubility after protonation with dilute acid, hence allowing accurate structural analysis by NMR spectroscopy.[11] 6AC-100, which is one of the three curdlan derivatives with full C6-amination, was selected for further chemical modifications and investigation of the gene/siRNA delivery efficiency. The 6-azide group can also directly react with alkyne through "click" chemistry.[12] The alkyne-functionalized lysine residues were conjugated to 6-azide-curdlan to give a cationic polymer. When complexed with plasmid DNA, the lysine-functionalized cationic polymer formed nanoparticles, which successfully delivered a plasmid expressing green fluorescence protein in HepG2 cells.

The advantages of such a chemically modified nucleic acid carrier are not only viable synthesis and access of the materials but also potentials for applications in tissue- or cell-targeted drug delivery. For example, partially aminated curdlan derivatives (such as 6AC-70, 6AC-50, etc.) may partially maintain the

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Traditional Mongolian medicine Eerdun Wurile improves stroke recovery through regulation of gene expression in rat brain

Saren Gaowa[a,b,c], Narisi Bao[a,b], Man Da[c], Qiburi Qiburi[d], Tsogzolmaa Ganbold[d], Lu Chen[d], Altanzul Altangerel[d], Temuqile Temuqile[b,c,*], Huricha Baigude[d,**]

[a] School of Basic Medical Science, Beijing University of Chinese Medicine, Chaoyang District, Beijing 100029, PR China
[b] Inner Mongolia Medical University, Hohhot, Inner Mongolia 010020, PR China
[c] International Hospital of Mongolian Medicine, Hohhot, Inner Mongolia 010021, PR China
[d] Institute of Mongolian Medicinal Chemistry, School of Chemistry & Chemical Engineering, Inner Mongolia University, Hohhot, Inner Mongolia 010020, PR China

ARTICLE INFO

Chemical compounds studied in this article:
povidone-iodine (PubChem CID: 410087)
chloral hydrate (PubChem CID: 2707)
geniposide (PubChem CID: 107848)
(+)-(7 S,8 R,8′R)-lyoniresinol 9-O-β-D-(6″-O-trans-sinapoyl) glucopyranoside (PubChem CID: 10395492)
3,5-di-O-caffeoylquinic acid (PubChem CID: 6474310)
kaempferol-3-O-rutinoside (PubChem CID: 24211973)
myristicin (PubChem CID: 4276)
costunolide (PubChem CID: 6436243)
isoliquiritigenin (PubChem CID: 638278)
toosendanin (PubChem CID: 115060)
4-dihydro-2-(4′ - hydroxyphenylmethyl) − 6 - [(3″,4″ -dihydroxy-5″- methoxyphenyl) methylene]-pyran-3, 5-dione
2,3- dihydro-2-(4′- hydroxy-phenylethyl)-6-[(3″,4″ -dihydroxy-5″-methoxy) phenyl]-5-pyrone

Keywords:
Ischemic stroke
Mongolian medicine
Eerdun Wurile
RNA-seq
Igf2
Microglia

ABSTRACT

Ethnopharmacological relevance: Eerdun Wurile (EW) is one of the key Mongolian medicines for treatment of neurological and cardiological disorders. EW is ranked most regularly used Mongolian medicine in clinic. Components of EW which mainly originate from natural products are well defined and are unique to Mongolian medicine.

Aim of the study: Although the recipe of EW contains known neuroactive chemicals originated from plants, its mechanism of action has never been elucidated at molecular level. The objective of the present study is to explore the mechanism of neuroregenerative activity of EW by focusing on the regulation of gene expression in the brain of rat model of stroke.

Materials and methods: Rat middle cerebral artery occlusion (MCAO) models were treated with EW for 15 days. Then, total RNAs from the cerebral cortex of rat MCAO models treated with either EW or control (saline) were extracted and analyzed by transcriptome sequencing. Differentially expressed genes were analyzed for their functions during the recovery of ischemic stroke. The expression level of significantly differentially expressed genes such as growth factors, microglia markers and secretive enzymes in the lesion was further validated by RT-qPCR and immunohistochemistry.

Results: Previously identified neuroactive compounds, such as geniposide (Yu et al., 2009), myristicin (Shin et al., 1988), costunolide (Okugawa et al., 1996), toosendanin (Shi and Chen, 1999) were detected in EW formulation. Bederson scale indicated that the treatment of rat MCAO models with EW showed significantly lowered neurological deficits ($p < 0.01$). The regional cerebral blood circulation was also remarkably higher in rat MCAO models treated with EW compared to the control group. A total of 186 genes were upregulated in the lesion of rat MCAO models treated with EW compared to control group. Among them, growth factors such as Igf1 ($p < 0.05$), Igf2 ($p < 0.01$), Gm ($p < 0.01$) were significantly upregulated in brain after treatment of rat MCAO models with EW. Meanwhile, greatly enhanced expression of microglia markers, as well as complementary components and secretive proteases were also detected.

Conclusion: Our data collectively indicated that EW enhances expression of growth factors including Igf1 and Igf2 in neurons and microglia, and may stimulate microglia polarization in the brain. The consequences of such activity include stimulation of neuron growth, hydrolysis and clearance of cell debris at the lesion, as well as the angiogenesis.

Abbreviations: tPA, tissue plasminogen; MCAO/R, middle cerebral artery occlusion/reperfusion; EW, Eerdun Wurile; NGF, nerve growth factor; BDNF, brain-derived neurotrophic factor; DEGs, differentially expressed genes; Igf2, insulin-like growth factor 2; IGFBP2, insulin-like growth factor binding protein 2; Tgf-b1, transforming growth factor beta 1; Vim, vimentin; Grn, granulin; ApoD, apolipoprotein D; Aif1, allograft inflammatory factor 1; Csf1r, colony stimulating factor 1 receptor; CX3CR1, C-X3-C motif chemokine receptor 1; C3, complementary component 3; C1qa, complementary component 1, q subcomponent, A chain

* Corresponding author at: International Mongolian Hospital, Hohhot 010021, PR China.
** Corresponding author.
E-mail address: hbaigude@imu.edu.cn (H. Baigude).

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