

CURRICULUM VITAE

S.M. Rajesh Kotcherlakota, Ph.D

Division of Applied Biology

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EDUCATION QUALIFICATION

Course	Institute & University	Year
Ph.D. Biological Sciences	CSIR- Indian Institute of Chemical Technology, Hyderabad	2019
M. Sc. (Biotechnology)	Andhra University , Visakhapatnam, India (8.56 CGPA)	2012
B. Sc.	Andhra University, Visakhapatnam (8.90 CGPA)	2010

RESEARCH EXPERIENCE

Position	Institute	Year
CSIR-SRF	CSIR- Indian Institute of Chemical Technology, Hyderabad	2016-2019
CSIR-SPF	CSIR- Indian Institute of Chemical Technology, Hyderabad	2015-2016
CSIR-PA-II	CSIR- Indian Institute of Chemical Technology, Hyderabad	2013-2015
Lecturer	DNR College of PG Courses and Research Centre	2012-2013

RESEARCH SKILLS

- **Nanotechnology:** Synthesis, fabrication and development of inorganic nanomaterials (gold, silver and platinum nanoparticles) and development of targeted nanoconjugation using plasmid DNA, siRNA, antibodies and anticancer drugs etc.
- **Green chemistry:** Bio-synthesis of metal nanoparticles using plant extracts and their therapeutic applications.
- **Analytical techniques:** Physico-chemical characterization of nanomaterials using UV Visible spectroscopy, XRD, FTIR, TEM, SEM techniques.
- **Molecular biology techniques:** DNA and RNA isolation, recombinant plasmid DNA isolation, primer designing, PCR, gene expression, purification of His tagged proteins, gel binding assays
- **Protein biochemistry techniques:** Protein estimation, SDS-PAGE, Western blotting and ELISA.
- **Microbiology:** Culturing various bacterial strains, bacterial transformation and measuring anti-bacterial activity using assays such as minimum inhibition concentration (MIC), zone of inhibition assays
- **In vitro studies:** Culture and maintenance of various mammalian cell lines (cancer: A549, SK-OV-3, B16F10, SK-BR-3, MDA-MB-231, MCF-7 and GL-261 and normal: CHO, NIH-3T3, HEK-293, COS-1 and HUVEC)

- **In vitro cell culture assays:** Cell viability/proliferation (MTT, SRB, tryphan blue, BrDU and thymidine incorporation), cell cycle analysis using FACS, immunofluorescence, cell migration (scratch/ wound healing), gene transfection, apoptosis estimation, FACS and fluorescence based cell uptake studies
- **Ex vivo:** Chick embryo angiogenesis
- **In vivo studies:** Establishment of xenografts in nude mice, syngenic tumor models in C57BL6 mice, administration of treatments to mice through various routes (intra-peritoneal, oral gavage and subcutaneous etc), animal imaging using *In vivo* imager, biodistribution studies immunohistochemistry, isolation of RNA from tumor tissues, TUNEL assay, and western blot from tumor lysates.
- **Toxicity and pharmacokinetics:** Sub-acute toxicity studies, pharmacokinetics studies of nanomaterials in blood, urine and feces in mouse models.

PUBLICATIONS (All research articles are from refereed, indexed and international high impact journals)

1. **Rajesh Kotcherlakota**, Durga Jeyalakshmi Srinivasan, Sudip Mukherjee, Mohamed Mohamed Haroon, Ghulam Hassan Dar, Uthra Venkatraman, Chitta Ranjan Patra and Vijaya Gopal, Engineered fusion protein-loaded gold nanocarriers for targeted co-delivery of doxorubicin and erbB2-siRNA in human epidermal growth factor receptor-2+ ovarian cancer, *Journal of Material Chemistry B*, 2017,5, 7082-7098. IF# 4.776
2. **Rajesh Kotcherlakota**, Ayan K. Barui, Sanjiv Prashar, Mariano Fajardo, David Briones, Antonio Rodríguez-Diéguez, Chitta R. Patra, and Santiago Gómez-Ruiz. Curcumin loaded mesoporous silica: an effective drug delivery system for cancer treatment. *RSC Biomaterials Science*, 2016, 4, 448-459. IF# 5.831
3. Suresh Kumar Gulla, **Rajesh Kotcherlakota**, Sahithi Nimushakavi, Narendra Varma Nimmu, Sara Khalid, Chitta Ranjan Patra, and Arabinda Chaudhuri. Au-CGKRK Nanoconjugates for Combating Cancer through T-Cell-Driven Therapeutic RNA Interference, *ACS Omega*, 2018, 3 (8), 8663–8676. (Euqal contribution first author)
4. K. Appalanaidu, **Rajesh Kotcherlakota**, T. L. Dadmal, Vishnu Sravan Bollu, Ravindra M. Kumbhare, Chitta Ranjan Patra Synthesis and biological evaluation of novel 2-imino-4-thiazolidinone derivatives as potent anti-cancer agents, *Bioorganic & Medicinal Chemistry Letters*, 26, 2016, 5361-5368. (Euqal contribution first author) IF# 2.442
5. Bonda Rama Rao, **Rajesh Kotcherlakota**, Susheel Kumar Nethi, Nagaprasad Puvvada, Bojja Sreedhar, Arabinda Chaudhuri, and Chitta Ranjan Patra. Ag₂[Fe(CN)₅NO] Nanoparticles Exhibit Antibacterial Activity and Wound Healing Properties. *ACS Biomaterial Science and Engineering*, 2018, 4 (9), 3434–3449. IF# 4.432
6. Sudip Mukherjee, Debabrata Chowdhury, **Rajesh Kotcherlakota**, Sujata Patra, Vinothkumar B, Manika Pal Bhadra, Bojja Sreedhar and Chitta Ranjan Patra. Potential theranostics application of bio-synthesized silver nanoparticles (4-in-1 system). *Theranostics*, 2014, (4), 3, 316-335. IF# 8.712
This work has been highlighted in *Nature India* “Glow nanoparticles inhibit cancer cell growth” doi:10.1038/nindia.2014.

7. Sudip Mukherjee, Mamatha Dasari, Sumahitha Priyamvada, **Rajesh Kotcherlakota**, Vishnusravan bolu, Chitta Ranjan Patra. Biosynthesized gold nanoconjugates induce the inhibition of cancer cell proliferation through induction of oxidative stress and their *in vivo* toxicity studies. *Journal of Material Chemistry B*, 2015, 3(18):3820-3830. IF# 4.776
8. Chittaranjan Patra, Sudip Mukherjee, **Rajesh Kotcherlakota**. Biosynthesized silver nanoparticles: a step forward for cancer theranostics? *Nanomedicine*, (2014), 9(10), 1445–1448. IF# 5.005
9. Abhishek Pal, Anirban Ganguly, Sumit Chowdhuri, Md Yousuf, Avijit Ghosh, Ayan Kumar Barui, **Rajesh Kotcherlakota**, Susanta Adhikari, and Rajkumar Banerjee. Bis-Arylidene Oxindole–Betulinic Acid Conjugate: A Fluorescent Cancer Cell Detector with Potent Anticancer Activity *ACS Medicinal Chemistry Letters*, 2015, 6 (5), 612–616. IF# 3.794.

Review articles

1. **Rajesh Kotcherlakota**, Syed Tazib Rahaman, Chitta Ranjan Patra, Nanomedicine for cancer therapy using Autophagy: An Overview (Invited review article), Current Topics in Medicinal Chemistry, Special Thematic Issue of CTMC of Bentham science.
2. Sourav Das, **Rajesh Kotcherlakota**, Chitta Ranjan Patra, Non-Invasive Imaging Techniques of Metal Nanoparticles and Their Future Diagnostic Applications (As co-corresponding author) [Invited review article from Springer Medical Imaging Methods-Recent Trends]

Publications Under review/ To be communicated

1. **Rajesh Kotcherlakota**, Sahithi Nimushakavi, Sudip Mukherjee, Hari Chandana Yadavilli, and Chitta Ranjan Patra, Biosynthesized gold nanoparticles: *In vivo* study of near infra-red fluorescence (NIR) based bio-imaging and cell labeling applications (Under revision in ACS Biomaterials Science & Engineering)
2. **Rajesh Kotcherlakota**, Kalyan vydium, Durga Jeyalakshmi Srinivasan, Sudip Mukherjee, Vijaya Gopal and, Chitta Ranjan Patra, Cationic gold nanoparticle mediated targeted gene therapy for restoration of function of p53 in ovarian cancer ((Under revision in ACS Biomaterials Science & Engineering)
3. Sudip Mukherjee, **Rajesh Kotcherlakota**, Saketh Nuthi, Dwaipayan Bhattacharya, Kuncha Madhusudana, Sumana Chakravarty, Ramakrishna Sistla, Chitta Ranjan Patra Poly (N-vinyl-2-pyrrolidone)-stabilized silver hexacyanoferrate nanoparticles: A multifunctional biomedical nanosphere (To be communicated)
4. Sudip Mukherjee, **Rajesh Kotcherlakota**, Dwaipayan Bhattacharya, Sumana Chakravarty, Chitta Ranjan Patra Doxorubicin conjugated PEG-modified platinum nanoparticles for *in vitro* and *in vivo* cancer therapy (To be communicated)

Book Chapters

1. Ayan Kumar Barui, **Rajesh Kotcherlakota**, Chitta Ranjan Patra, Medicinal applications of metal nanoparticles. (**Metal Nanoparticles synthesis and Applications in Pharmaceutical Sciences**) provisionally accepted in Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany.

3. Ayan Kumar Barui, **Rajesh Kotcherlakota**, Chitta Ranjan Patra , Biomedical applications of zinc oxide nanoparticles, (**Composites in Biomedical Engineering**) in ELSEVIER, Limited.
4. Ayan Kumar Barui, **Rajesh Kotcherlakota**, Vishnu Sravan Bollu, Susheel Kumar Nethi, Chitta Ranjan Patra. Biomedical and drug delivery applications of functionalized inorganic nanomaterials. Elsevier; Wood head Publishing Limited. Drug Delivery and Biomedical Applications, 2017, Pages 325-379.
5. Sudip Mukherjee, Bonda Rama Rao, **Rajesh Kotcherlakota**, Chitta Ranjan Patra, Prussian blue nanoparticles and nanocomposites: Synthesis, devices and applications, Panstanford ISBN 9789814800051
6. **Rajesh Kotcherlakota**, Sourav Das, Chittaranjan Patra, Therapeutic Applications of Green Synthesized Silver Nanoparticles, Elsevier, Micro and Nano Technologies, 2019, Pages 389-428
7. Sahithi Nimushakavi, **Rajesh Kotcherlakota**, Shagufta Haque and Chitta Ranjan Patra, Applications of multifunctional carbon nanotubes in biology and medicine, (Elsevier): (Invited Book Chapter, In press)

Patents

1. **Rajesh Kotcherlakota**, Sudip Mukherjee, Chitta Ranjan Patra, Vijaya Gopal. Gold nanoparticles based new formulations for the delivery of drugs (CSIR reference number: 0202NF2016).
2. Ramarao Bonda, Susheel Kumar Nethi, **Rajesh Kotcherlakota**, Chitta Ranjan Patra, Design and synthesis of silver nitroprusside nanoparticles as effective anti-microbial and anti-cancer agents. (CSIR patent number: 2016 1103 9557).

List of conferences attended

1. Presented poster in **International Conference in Chemical Biology** (ICCB-2014) held at CSIR-IICT, Hyderabad.
2. Oral presentation in **International Conference “Integrative Biology & Applied Genetics”** (ICIBAG – 2018) conducted by Department of Genetics Osmania University, Telangana.
3. Oral presentation in **International Conference on Applied Science and Technology** (ICAST-2018) held at SRKR College, Bhimavaram, AP.
4. Participated in ‘**Indo – US Bilateral symposium on Nanotechnology & Regulatory Science**’ held at Hyderabad International Trade Expositions (HITEX) convention Centre, Hyderabad.
5. Participated in ‘**International Conference on Sustainable Chemistry for Health Environment and Materials**’ held at CSIR-IICT, Hyderabad

Awards/ Achievements

1. **K.V. Rao Researcher Award** in Biological Sciences in the year 2017-18 from K.V. Rao Scientific Society, Hyderabad.
2. **Best Oral Presentation Award** Topic 'Gold nanoparticles based combinatorial-targeted approach for the treatment of ovarian cancer' at International Conference on Applied Science and Technology (ICAST-2018) held at SRKR College, Bhimavaram, A.P.
3. Awarded gold medal for highest scorer in M. Sc. Biotechnology.
4. Awarded Gold Medal for Highest Score in B. Sc. Botany.
5. Received 44th rank in AURPGCET-2010.
6. Awarded Smt. G. Merit Award for Highest Scorer in Intermediate.
7. Awarded Dr. Rmana Rao & Smt. Varahamma Merit Award for Highest Scorer in Intermediate.

Personal profile

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References

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Engineered fusion protein-loaded gold nanocarriers for targeted co-delivery of doxorubicin and erbB2-siRNA in human epidermal growth factor receptor-2+ ovarian cancer†

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Designed recombinant proteins comprising functional domains offer selective targeting of cancer cells for the efficient delivery of therapeutic agents. The efficacy of these carriers can be further enhanced by conjugating engineered proteins to nanoparticle surfaces. However, recombinant protein-loaded nanoparticle-based drug delivery systems are not well addressed for ovarian cancer therapy. In the present study, using a combinatorial approach, we designed and fabricated a drug delivery system by combining gold nanoparticles (AuNPs) with an engineered bi-functional recombinant fusion protein TRAF(C) (TR), loaded with an anticancer drug, namely doxorubicin (DX), and erbB2-siRNA (si), to mediate target specific delivery into SK-OV-3, a model human ovarian cancer cell line over expressing HER2 receptors (*i.e.* human epidermal growth factor receptor-2). The nanoparticle-based targeted drug delivery system, designated as TDDS (Au-TR-DX-si), was found to be stable and homogenous as revealed by physicochemical and biochemical studies *in vitro*. In addition, TDDS was functional upon evaluation *in vivo*. Intraperitoneal administration of TDDS at 2.5 mg kg⁻¹ of DX and 0.25 mg kg⁻¹ of erbB2 siRNA into SK-OV-3 xenograft nude mice, revealed target specific uptake and consequent gene silencing resulting in significant tumor suppression. We attribute these results to specific co-delivery of erbB2 siRNA and DX mediated by TDDS into SK-OV-3 cells via HER2 receptors. Additionally, the biodistribution of TDDS, as quantitated by ICP-OES, confirmed tumor-specific accumulation of AuNPs primarily in tumor tissues, which firmly establishes the efficacy of the nanomedicine-based combinatorial approach for the treatment of ovarian cancer in a non-toxic manner. Based on these findings, we strongly believe that the nanomedicine-based combinatorial approach can be developed as a universal strategy for treatment of HER2+ ovarian cancers.

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Introduction

Cancer is a global health problem.¹ Among all cancers, ovarian cancer is the most common malignancy in women with poor prognosis, usually diagnosed after stage III/IV.^{2–4} For example,

in the United States alone, 21 290 new cases were identified in women with ovarian cancer and 14 180 death cases were recorded.¹ Traditional therapies for the treatment of ovarian cancer comprise surgery, chemotherapy and radiation therapy, to name a few.^{5,6} Among these, chemotherapy is highly sought as a popular approach,⁷ although a major limitation is non-specificity and poor bioavailability that leads to toxicity and low efficacy. It is increasingly evident that nanotechnology plays a vital role in the systemic delivery of drugs and nucleic acids to malignant cells in a targeted manner.⁸ Such strategies synergistically reduce the toxicity of the anti-cancer drug while increasing the therapeutic efficacy.⁸ Nanomedicine approaches widely employ AuNPs in gene and drug delivery due of their unique fundamental properties (chemical, physical, electrical, optical), surface plasmon resonance (SPR), tunable size, ease of synthesis and surface functionalization. Moreover, a long

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‡ Equal contribution.



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Curcumin loaded mesoporous silica: an effective drug delivery system for cancer treatment†

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In the present study, we report the delivery of anti-cancer drug curcumin to cancer cells using mesoporous silica materials. A series of mesoporous silica material based drug delivery systems (**S2**, **S4** and **S6**) were first designed and developed through the amine functionalization of KIT-6, MSU-2 and MCM-41 followed by the loading of curcumin. The curcumin loaded materials were characterized with several physico-chemical techniques and thoroughly screened on cancer cells to evaluate their *in vitro* drug delivery efficacy. All the curcumin loaded silica materials exhibited higher cellular uptake and inhibition of cancer cell viability compared to pristine curcumin. The effective internalization of curcumin in cancer cells through the mesoporous silica materials initiated the generation of intracellular reactive oxygen species and the down regulation of poly ADP ribose polymerase (PARP) enzyme levels compared to free curcumin leading to the activation of apoptosis. This study shows that the anti-cancer activity of curcumin can be potentiated by loading onto mesoporous silica materials. Therefore, we strongly believe that mesoporous silica based curcumin loaded drug delivery systems may have future potential applications for the treatment of cancers.

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www.rsc.org/biomaterialsscience

Introduction

Curcuma longa has extensively been used as a food additive and conservant in India, China and other Asian countries.¹ In addition, it has been used for domestic remediation in Chinese medicine for different diseases such as diabetes, hepatic dysfunctions and other health problems.² For this reason, during the last decades a high number of studies have been carried out in order to determine the biological activity and pharmacological properties of *Curcuma longa* and its extracts.³ Curcumin is the major curcuminoid and the main bioactive component of *Curcuma longa*. It has diverse biological applications as an antioxidant, antimutagenic, antidiabetic, antibacterial, antifungal and especially as an anticancer

agent.⁴ Curcumin has also been used in clinical trials for the reduction of the inflammatory processes after surgery.⁵ Furthermore, earlier reports demonstrate that curcumin is cytotoxic to various cancer cells through the induction of apoptosis and decrease of cell invasiveness of the tumoural area.⁶ Dose dependent toxicity studies in normal cell lines suggest that curcumin is well tolerated at high doses without any toxic effect. However, the administration of curcumin in the human body as an anti-cancer agent has not been found to be effective due to its lower systemic bioavailability originating from its low solubility and instability.⁷ To overcome these limitations, researchers have been engaged in making different formulations such as the encapsulation of curcumin with polymeric nanoparticles or silicalization of curcumin-loaded solid lipid nanoparticle (SLN)/micelle dispersions,⁸ metal or non-metal nanoparticles, phospholipids, microemulsions or by the preparation of other curcumin analogues.⁹ Amongst all these approaches, the prevalent one is the encapsulation of curcumin with nanoparticles. However, rigorous studies are still needed to evaluate the efficacy and toxicity of the nanoparticles.^{10a,b}

A different approach for developing novel drug-delivery systems is the use of mesoporous silica materials because of their interesting properties, such as (i) variable and controllable particle sizes ranging from 50 nm to microns that lead to an easy endocytosis by cells and possess low cytotoxicity,

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Au-CGKRK Nanoconjugates for Combating Cancer through T-Cell-Driven Therapeutic RNA Interference

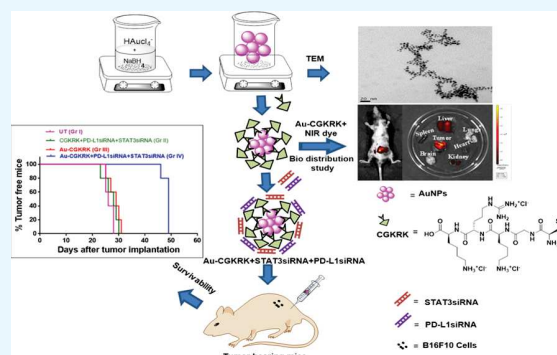
Suresh Kumar Gulla,^{†,§,||} Rajesh Kotcherlakota,^{†,§,||} Sahithi Nimushakavi,^{†,§} Narendra Varma Nimmu,[‡] Sara Khalid,[‡] Chitta Ranjan Patra,^{*,†,§,||} and Arabinda Chaudhuri^{*,†,§,||}

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Supporting Information

ABSTRACT: Numerous prior studies on fighting cancer have been based on using inhibitors of JAK-STAT pathway (signal transducer and activator of transcription 3 (STAT3) inhibitor in particular), a signaling pathway responsible for progression of many types of cancer cells. However, recent studies have shown that STAT3 activation leads to upregulation of program death receptor-ligand 1 (PD-L1, an immune checkpoint protein that plays a major role behind evasion of immune systems by growing tumors) expression levels in tumor cells, leading to enhanced immune suppression. This is why global efforts are being witnessed in combating cancer through use of immune checkpoint inhibitors. Herein, we report on the design, synthesis, physicochemical characterizations, and bioactivity evaluation of novel tumor- and tumor-vasculature-targeting noncytotoxic Au-CGKRK nanoconjugates (17–80 nm) for combating tumor. Using a syngeneic mouse tumor model, we show that intraperitoneal (i.p.) administration of the Au-CGKRK nanoparticles (NPs) complexed with both PD-L1siRNA (the immune checkpoint inhibitor) and STAT3siRNA (the JAK-STAT pathway inhibitor) results in significant (>70%) enhancement in overall survivability (OS) in melanoma-bearing mice ($n = 5$) when compared to the OS in the untreated mice group. The expression levels of CD8 and CD4 proteins in the tumor lysates of differently treated mice groups (by Western blotting) are consistent with the observed OS enhancement being a T-cell-driven process. Biodistribution study using near-infrared dye-loaded Au-CGKRK nanoconjugates revealed selective accumulation of the dye in mouse tumor. Notably, the overall survival benefits were significantly less (~35%) when melanoma-bearing mice were treated (i.p.) with Au-CGKRK NPs complexed with only PD-L1siRNA or with STAT3siRNA alone. The presently described Au-CGKRK nanoconjugates are expected to find future use in therapeutic RNA-interference-based cancer immunotherapy.



1. INTRODUCTION

Many of the contemporary cancer treatment modalities including chemotherapy, radiation therapy, surgery, etc. suffer from severe toxic side effects. They not only kill cancer cells but also, due to their nonselective nature, kill noncancerous healthy body cells. Global efforts are being witnessed toward developing tumor-cell-selective treatment strategies for combating cancer. High-affinity ligands for receptors overexpressed on tumor cells are being covalently tethered to the exosurfaces of various biocompatible drug carriers (with loaded drugs) such as biodegradable and injectable polymer-based sustained release microparticles,^{1–3} cyclodextrin-based systems,^{4–6} dendrimers,^{7,8} gold-mesoporous silica hybrid theranostics,⁹ silk-fibroin nanoparticles,¹⁰ liposomes,^{11–17} and metal-based nanoparticles.^{18,19}

The signal transducer and activator of transcription 3 (STAT3) is a transcription factor that plays a pivotal role in tumor cell proliferation²⁰ being constitutively activated

(phosphorylated) in numerous cancer cells. In consequence, STAT3 is emerging as an important target in cancer therapy either through use of RNA interference (RNAi, using STAT3siRNA) or using small-molecule inhibitors of STAT3 phosphorylation such as SU54, WP1066, AG490, curcumin, and analogues of curcumin.^{20–24}

Our immune cells fail to eliminate tumor cells because growing tumors develop strategies to evade our immune system. Such immune evasion happens through immune checkpoint interactions between programmed death receptor 1-ligand 1 (PD-L1) expressed on tumor cells and programmed death receptor 1 (PD-1) on the surface of T-cells (an interaction that inhibits proliferation of cytotoxic T-cells).^{25,26} This is why unprecedented global efforts are being witnessed in

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Ag₂[Fe(CN)₅NO] nanoparticles exhibit anti-bacterial activity and wound healing properties

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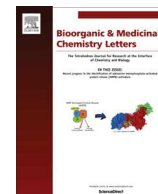
ABSTRACT:

Therapeutic agents harboring both wound healing and antibacterial activities have much demand in biomedical applications. Development of such candidates with clinically approved materials adds more advantages towards these applications. Recently, silver metal complex nano-materials have been playing a major role in medical uses especially for anti-bacterial activity and wound healing. In this report, we designed and synthesized silver nitroprusside complex nanoparticles (abbreviated as AgNNPs) using sodium nitroprusside and silver nitrate (both are FDA approved precursors). The nanoparticles (AgNNPs) were thoroughly characterized by various physico-chemical techniques such as XRD, FTIR, TGA, DLS, EDAX, Raman, ICP-OES, HRTEM and FESEM. The cell viability assay in normal cells (EA.hy 926 cells, NIH 3T3) using MTT reagents and CEA assay (CEA: Chick embryo angiogenesis assay) in fertilized eggs demonstrate the biocompatibility of AgNNPs. These nanoparticles show effective antibacterial activity against both Gram positive and Gram negative bacteria through membrane and DNA damage. Additionally, AgNNPs accelerate the wound healing in C57BL6 mice by altering the



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Synthesis and biological evaluation of novel 2-imino-4-thiazolidinone derivatives as potent anti-cancer agents



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Reactive oxygen species (ROS)

ABSTRACT

A new series of 2-imino-4-thiazolidinone derivatives (**7a–7t**) has been synthesised and screened for their cytotoxicity against three cancer cell lines (B16F10, A549, PANC-1) and normal cell line (CHO). Among the compounds tested, compounds **7k**, **7m**, **7n** showed potent cytotoxicity against B16F10 cell line with IC₅₀ between 3.4 and 7 μM. Interestingly these three compounds are non toxic to non cancerous CHO cells and induced apoptosis in B16F10 cells observed by DNA damage analysis through PI/Hoechst double staining method. Compounds **7k** and **7n** induced G0/G1 cell cycle arrest while compound **7m** induced G2/M cell cycle arrest in B16F10 cells which confirms that these compounds have role in cancer cell cycle regulation. Additionally, compound **7m** showed generation of intracellular reactive oxygen species (ROS) in B16F10 cells that may contribute in the cell cycle arrest whereas compounds **7k** and **7n** show anti-cancer activity through independent of ROS formation. Induction of apoptosis, cell cycle arrest in B16F10 cells are found to be the anti-cancer mechanism of these three compounds. The results all together demonstrate the potent cytotoxic nature of these compounds in cancer cells could be considered as new class of chemotherapeutic agents in near future.

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Cancer is one of the leading causes of death in the world.¹ Genotoxicity and cytotoxicity of anti-cancer drugs to the normal tissues is major problems in cancer therapy and produces the risk of inducing secondary malignancy as well as leads to many side effects. Among the various therapies such as surgery, chemotherapy, radiation and monoclonal antibody therapy,² chemotherapy is a most common treatment for all type of cancers. In clinics, new combination of chemotherapeutic drugs has been used for the better treatment of different cancers. However, cancer research always requires the discovery of new drugs that can kill the cancer cells or stop the growth of cancer cells more specifically and overcome the limitation of toxicity to normal tissue which leads to many side effects. In order to develop drugs with such capabilities, scientists have focused upon many different aspects of cancer

biology during their research. In this framework, five-member ring, 4-thiazolidinone derivatives have attracted much attention over the years since it is a significant and versatile scaffold that has occupied a prominent position in medicinal chemistry.³ The detailed literature survey of 4-Thiazolidinone and its derivatives demonstrated a wide broad spectrum pharmacological properties such as anti-microbial,^{4a,b} anti-malarial,^{5a,b} anti- HIV,^{6a,b} anti-inflammatory,^{7a–c} anti-oxidant,^{8a,b} anti-tuberculostatic^{9a,b} and COX-2 inhibitor activities.¹⁰ Various researchers have documented the progress of this scaffold through chemical modifications.^{11–17} Among the thiazolidinone derivatives, substituted 4-Thiazolidinone such as MKT-077, 1-ethyl-2-[[3-ethyl-5-(methylbenzothiazolin-2-ylidene)-4-oxothiazolidin-2-ylidene]methyl]pyridinium chloride **I** (Fig. 1) (formerly known as FJ-776) know for anti-proliferative activity against cancer cell lines through its ability to inhibit members of the heat shock protein 70 (Hsp70) family of molecular chaperones. However, MKT-077 is rapidly metabolized, which limits its use as either a chemical probe or potential therapeutic. ALC 67 molecule **II** (Fig. 1), exhibit potent and selective in vitro antitumor properties in human cancer cell lines (example liver, colon, breast and endometrial cancer) which were also demonstrated to induce apoptosis by activating caspase-9.

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