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RESEARCH ARTICLE

Transferrin receptor-targeted vitamin E TPGS micelles for brain cancer therapy: preparation, characterization and brain distribution in rats

Sonali[1], Poornima Agrawal[1], Rahul Pratap Singh[1], Chellappa V. Rajesh[2], Sanjay Singh[3], Mahalingam R. Vijayakumar[3], Bajrangprasad L. Pandey[1], and Madaswamy Sona Muthu[1]

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Abstract

The effective treatment of brain cancer is hindered by the poor transport across the blood–brain barrier (BBB) and the low penetration across the blood–tumor barrier (BTB). The objective of this work was to formulate transferrin-conjugated docetaxel (DTX)-loaded D-alpha-tocopheryl polyethylene glycol 1000 succinate (vitamin E TPGS or TPGS) micelles for targeted brain cancer therapy. The micelles with and without transferrin conjugation were prepared by the solvent casting method and characterized for their particle size, polydispersity, drug encapsulation efficiency, drug loading, *in vitro* release study and brain distribution study. Particle sizes of prepared micelles were determined at 25 °C by dynamic light scattering technique. The external surface morphology was determined by transmission electron microscopy analysis and atomic force microscopy. The encapsulation efficiency was determined by spectrophotometery. *In vitro* release studies of micelles and control formulations were carried out by dialysis bag diffusion method. The particle sizes of the non-targeted and targeted micelles were <20 nm. About 85% of drug encapsulation efficiency was achieved with micelles. The drug release from transferrin-conjugated micelles was sustained for >24 h with 50% of drug release. The *in vivo* results indicated that transferrin-targeted TPGS micelles could be a promising carrier for brain targeting due to nano-sized drug delivery, solubility enhancement and permeability which provided an improved and prolonged brain targeting of DTX in comparison to the non-targeted micelles and marketed formulation.

Keywords

Brain distribution, brain tumor, cancer nanotechnology, drug release, micelles, vitamin E TPGS

History

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Introduction

Brain cancer is one of the most difficult challenges in oncology affecting many people worldwide. According to a report, in the USA, the incidence of primary brain tumors is 7–8 per 100 000, and it is expected that over 23 000 new cases will be diagnosed every year. Among different types of brain cancer, glioma is the most prevalent and aggressive type in adults with a survival time of 12–15 months and a 5-year survival rate of <5% (Cui et al., 2013; Burgo et al., 2014; Gaillard et al., 2014). Despite the development of chemotherapy, median survival span of brain cancer patients (i.e. 1 year) has not been significantly improved. The reduced efficacy of brain cancer chemotherapy is mainly attributed to the existence of blood–brain barrier (BBB), which limits the penetration of drug molecules into brain given systemically (Ren et al., 2010). Another obstacle is blood–tumor barrier (BTB), which hampers drug accumulation and uptake, results in poor drug accumulation in brain tumor (Cui et al., 2013).

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To target, the anti-cancer drug into the brain is one of the most challenging areas of research for drug delivery scientists (Kulkarni & Feng, 2011; Wohlfart et al., 2012; Muthu et al., 2014a,b). Since the efficiency of BBB penetration of anti-cancer drug is low, higher doses are needed to achieve a desired therapeutic effect, which usually produce unwanted side-effects (Alam et al., 2010; Gan & Feng, 2010). To solve these problems, many drug-targeting and delivery strategies to the brain cancer have been discovered and developed in view of manipulating endogenous transport systems to overcome the BBB without physically interfering with the brain tissues (Béduneaua, 2007; Jones & Shusta, 2007; Wohlfart et al., 2012; Yue et al., 2012). Mainly, many nanocarriers are under investigation such as albumin nanoparticles, gelatine nanoparticles, nanoconjugates, polymeric nanoparticles, solid–lipid nanoparticles, carbon nanotubes, micelles and liposomes (Muthu et al., 2009; Muthu & Feng, 2009, 2010; Muthu & Singh, 2009; Muthu & Wilson, 2010; Muthu et al., 2014a).

Among all nanocarriers, micelles have attracted much attention as a targeted drug carrier in recent years. Micelles are amphiphilic spherical nanostructures consisting of a hydrophobic core and a hydrophilic shell. It has many

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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Design and development of oxobenzimidazoles as novel androgen receptor antagonists

R. Elancheran[1] · K. Saravanan[2] · Bhaswati Choudhury[1] · S. Divakar[3] · S. Kabilan[2] · M. Ramanathan[3] · Babulal Das[4] · R. Devi[1] · Jibon Kotoky[1]

Received: 5 February 2015 / Accepted: 6 January 2016 / Published online: 21 January 2016

Abstract Antiandrogens are a novel class of anticancer agents that inhibit cancer cell proliferation and induce apoptosis in various cell lines. To find the lead compound from the oxobenzimidazole derivatives, receptor-ligand docking studies were initially performed using Schrödinger software. The best fit molecules were synthesized and characterized through IR, ^{1}H-NMR, ^{13}C-NMR and HRMS analyses. The structure of compound **(9b)** was further confirmed by single-crystal XRD analysis. The cell viability of the compounds was determined by MTT assay to find IC_{50} values against prostate cancer and breast cancer cell lines (PC-3, LNCaP, MCF-7 and MDA-MB-231). The ADME/T property studies were performed to rationalize the inhibitory properties of these compounds. It can be concluded from the study that **9b** is the most active compound from the series against PC-3 and LNCaP cell lines.

Keywords Androgen receptor · Prostate cancer · Antiandrogen · Breast cancer · Oxobenzimidazoles

Electronic supplementary material The online version of this article (doi:10.1007/s00044-016-1504-3) contains supplementary material, which is available to authorized users.

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Introduction

Androgen receptor (AR), belongs to the nuclear receptor subfamily, plays an important role in the development, growth, function and homeostasis of the prostate. The National Cancer Institute (NCI) has estimated that 220,800 men will be diagnosed with and 27,540 men will die of prostate cancer in the USA in 2015 (Ferlay *et al.,* 2010; Howlader *et al.,* 2015). Recently, we reported that AR is one of the attractive targets to treat prostate cancer (PCa) (Elancheran *et al.,* 2015b). Although androgens are often considered to be "male" hormones, they are also found at lower levels in women. Recent studies have found that AR is frequently expressed in primary breast tumors, is estimated to be 50–90 %, depending on the subtypes of breast cancer, and could respond to antiandrogen treatment (Fioretti *et al.,* 2014). Antiandrogens, such as bicalutamide (Chen *et al.*, 2005; Gao *et al.*, 2006), cyproterone acetate (Figg *et al.,* 2010; Neumann and Töpert, 1986), flutamide (Cleve *et al.,* 2011; Brogden and Clissold, 1989) and nilutamide (Hsieh and Ryan, 2008; Moguilewsky *et al.,* 1987; Kassouf *et al.,* 2003) have been used to block the androgen signal, but they have several side effects. Recently, novel AR antagonist, enzalutamide (Scher *et al.,* 2010; Tran *et al.,* 2009), has demonstrated efficacy against castration-resistant prostate cancer (CRPC) and estrogen receptor-negative tumors. Among the subtypes, triple-negative breast cancers (ER-, PR-, HER2-) were positive for AR expression and may respond to treatment with antiandrogen drugs (Ni *et al.,* 2011). ARN-509 (IC50 = 16 nmol/L) binds AR with seven to tenfold greater affinity than the clinically approved antiandrogen, bicalutamide (median IC_{50} = 160 nmol/L), and competes for the same binding site in the ligand-binding pocket of the receptor (Clegg *et al.,* 2012). As a result, there is an

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BENTHAM SCIENCE

Production of Irbesartan Nanocrystals by High Shear Homogenisation and Ultra-Probe Sonication for Improved Dissolution Rate

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H. Rahman

Abstract: Irbesartan (IRB) is a BCS class II drug with poorly aqueous solubility and its absorption is dissolution rate limited. In the present study solubility and dissolution rate of IRB were improved by nanonization and using two poly(ethylene oxide)-*b*-poly(propylene oxide)-*b*-poly(ethylene oxide) amphiphiles, namely Pluronic® F127 and Pluronic® F68, as nanosuspension stabilisers. In addition, the role of these surfactants in the solubilization of the drug was assessed. The nanocrystals were produced by two top-down techniques- high shear homogenisation and ultra-probe sonication. The nanocrystals were characterized for particle size, size distribution and zeta potential and compared to the unprocessed drug by FTIR, thermal analysis, scanning electron microscopy, solubility and dissolution rate. IRB nanocrystals showed greater solubility and faster dissolution rate than the original drug, solubility being higher for formulations prepared with F127 than those with F68. Presence of an endothermic peak of drug in the formulation confirmed its crystalline nature, regardless of the use of two energetic methods. SEM of the nanocrystals revealed a small rod-shaped morphology and the substantial decrease of the particles size. Overall results support these nanonization techniques as a simple, cost-effective and scalable approach to improve the aqueous solubility of drugs such as IRB that are classified into Class II of the Biopharmaceutic Classification System (BCS).

Keywords: Drug dissolution rate, drug solubility, Irbesartan nanocrystals, Pluronic® F127 and Pluronic® F68, top-down nanonization.

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1. INTRODUCTION

Approximately 50-70% of the approved and experimental drugs are classified into Class II of the Biopharmaceutic Classification System (BCS), *i.e.* low solubility and high permeability [1]. These drugs are dissolution rate limited and their oral bioavailability could be improved by increasing their aqueous solubility and dissolution rate. With this aim, many nanoformulation approaches have been introduced in recent years. Nanosuspensions [2], self-emulsifying drug delivery systems, self-microemulsifying drug delivery systems [3], cyclodextrin complexes [4] and lipidic and polymeric nanocarriers [5] are among the most extensively investigated.

Nanocrystal technology is one of the simplest and most promising methods to improve the solubility of drugs classified into Class II of the Biopharmaceutic Classification System (BCS). The method relies on the reduction of the drug particle size and the sharp increase of the surface area [6, 7] that results in a faster dissolution rate, as described by the Noyes-Whitney equation [8]. A remarkable advantage of drug nanocrystals is that they are "nanocarrier-less" systems that due to the high density display high drug content per total product weight. Drug nanocrystals can be produced by top-down or bottom-up techniques [9]. In the former, the particle size undergoes reduction by homogenisation/milling methods [10], while in the latter the drug is precipitated as nano-sized crystals in a variety of solvents/anti-solvent systems [7]. In both approaches, surfactants of different nature are used either in single form or in combination to physically stabilize the nanosuspension.

Top-down methods are more versatile than bottom-up ones as they are suitable for most drugs and are deprived of organic solvents that have increasingly become an environmental concern [10, 11]. The high-speed homogenisation and ultra probe sonication techniques are simple and feasible methods that can be employed for the preparation of drug nanocrystals [12]. The stabilizers used and their concentration play a key role in the formation of nanocrystals and their size and the physical stability of the produced nanosuspensions [13]. Poloxamers (known with brand name of Pluronic®) are thermo-responsive ampiphilic poly(ethylene oxide)-*b*-poly(propylene oxide)-*b*-poly(ethylene oxide) (PEO-PPO-PEO) block copolymers commercially available in various molecular weights and hydrophilic-lipophilic balances

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Original Research Article

Fetal Toxicity and Cytotoxicity of *Lannea kerstingii* Engl and *Krause* Stem Bark (*Anacardiaceae*)

Aboudoulatif Diallo[1]*, Paolo Darre[2], Kossi Metowogo[3], Povi Lawson-evi[3], Divakar Selva[4], Yao Potchoo[1], Edmond Creppy[5] and Muthiah Ramanathan[4]

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Abstract

Purpose: *To evaluate the fetal toxicity and cytotoxicity of L. kerstingii in pregnant rats exposed in the organogenic period.*
Methods: *Mated female rats were randomly assigned to three experimental groups of 8 animals each. Pregnant rats received orally 500 or 1000 mg/kg of 50 % hydroalcohol extract of L. kerstingii, daily from the 17th to the 20th day of gestation. On day 21 of pregnancy, the females were sacrificed. Laparotomy was performed and uterine horns were removed. The number of implants, resorptions, dead and live fetuses were then recorded. The ovaries were also observed and corpora lutea were counted. The cytotoxic effect of L. kerstingii hydroalcohol extract was evaluated on Caco-2 cell lines using MTT (3-(4, 5-dimetylthiazol-2-yl)-2, 5- diphenyltetrazolium bromide) and neutral red uptake assay.*
Results: *No visible signs of toxicity were observed in the female rats and their pups through-out the study period. However, L. kerstingii (500 and 1000 mg/kg) caused a significant de-crease ($p < 0.01$) in fetal weight compared with control. With regard to implantation, resorption and mortality, there was no significant difference between groups. L. kerstingii hydroal-cohol extract (IC_{50}, 29 µg/mL) was more cytotoxic than the aqueous extract (IC_{50}, 141 µg/mL).*
Conclusion: *The administration of hydroalcohol extract of L. kerstingii to female rats in late pregnancy is toxic to the fetus.*

Keywords: *Lannea kerstingii, Fetal toxicity, Cytotoxicity, Mortality, Oxidative stress, Anorexia*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

The use of herbal plants as natural remedies, functional foods, and dietary supplements for health care has been increasing in the world. Market estimates suggest that the rate of growth in sales of traditional medicinal products in recent years is between 5 and 18 % per annum [1].

One of these traditional medicines is *Lannea kerstingii* Engl. And *K. Krause* (Anacardiaceae). *L. kerstingii* stem bark decoction gives a red color. Many women use it during pregnancy or during lactation in Togo to treat anaemia and malaria [2]. In West African countries such as Ivory coast, *L. kerstingii* stem bark and root are consumed as traditional remedies for the treatment of diarrhoea, gastritis, rheumatic, sterility, scorbut, scurvy, epilepsy and intestinal helminthiasis [3,4]. The fruit of *L. kerstingii* is eaten raw in Guinean pre-forest savannas of Ivory Coast [5]. In Benin, *L. kerstingii* leaves are used in the treatment of Buruli ulcer [6].

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In Vitro Anticancer Assessment of *Annickia chlorantha* (Oliv.) Setten & Maas Stem (Annonaceae) Bark from Democratic Republic of Congo

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Abstract

In this study, we evaluated the anti-cancer property of five bark extracts and the isolates from chloroform and ethyl acetate of *Annickia chlorantha* by the tetrazolium salt method (MTT method). The anti-cancer activity was performed on human prostate cancer cell lines PC-3 and hormone-dependent breast cancer cell lines MCF-7. Results indicated that the two isolates displayed interesting cytotoxicity towards MCF-7 cell lines with CC_{50} of 3.84 CC_{50}/mL and 4.87 CC_{50}/mL for chloroform and ethyl acetate respectively; while the total bark extracts showed CC_{50} of 24.33 CC_{50}/mL, 36.49 CC_{50}/mL and 73.52 CC_{50}/mL for chloroform, ethyl acetate and methanol extracts respectively. By the other hand on PC-3, the CC_{50} of the isolates were higher than the one on MCF-7, more than 10 CC_{50}/mL for both chloroform and ethyl acetate isolates and 49.14 CC_{50}/mL, 77.33 CC_{50}/mL, 89.38 CC_{50}/mL and 92.37 CC_{50}/mL, respectively for chloroform, ethyl acetate and methanol soluble extracts. From this study, we identified that the two isolates had anti-cancer properties against MCF-7 cell lines.

Keywords

***Annickia chlorantha*, Cancer, MCF-7 Cell Lines, PC-3 Cell Lines, Anti-Proliferative Compounds**

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No. NIS/6-34/Res/EMR/16-17 Dated:13-5-2016

To

Dr.M.Ramanathan,
Principal,
PSG College of Pharmacy,
Avinashi Road,
Peelamedu, Coimbatore-641004.

Sir,

Sub: Your letter dated 10-5-2016 – Permission for Dr.Manjiri as Co-Investigator – Reg.

Ref

I hereby permit Dr.Manjiri, M.D., Lecturer, National Institute of Siddha as Co-Investigator for formulation development with Siddha medicine on breast cancer and colon cancer subject to the compliance of the following conditions before submitting to any Department.

1. The proposal should be submitted for review of NIS
2. Routine duties of co-investigator should not be affected
3. No extra leave or facility given to co-investigator for the project work

Yours faithfully,

V. Banum

(Prof.Dr.V.Banumathi)
DIRECTOR

International Journal of Nanomedicine

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PERSPECTIVES

A brief perspective on the diverging theories of lymphatic targeting with colloids

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Abstract: For targeted delivery of colloids to the lymphatic system, the colloids should efficiently reach and remain in the lymphatics for a considerable period of time. As per the current knowledge, diffusion and phagocytosis are the two mechanisms through which colloids reach the lymphatic system. Several parameters including particle size and charge have been shown to affect the direct uptake of colloids by the lymphatic system. Although many researchers attached ligands on the surface of colloids to promote phagocytosis-mediated lymphatic delivery, another school of thought suggests avoidance of phagocytosis by use of carriers like polyethylene glycol (PEG)ylated colloids to impart stealth attributes and evade phagocytosis. In this perspective, we weigh up the paradoxical theories and approaches available in the literature to draw conclusions on the conditions favorable for achieving efficient lymphatic targeting of colloids.

Keywords: lymphatic targeting, colloids, PEGylation, phagocytosis

Introduction

The lymphatic system (lymphatics), which encompasses the circulating lymph, network of lymphatic pathways (lymphatic capillaries, collecting vessels, trunks, and ducts), and lymphatic organs (lymph nodes, thymus, bone marrow, tonsils, spleen, etc) is present throughout the body in conjunction with the systemic circulation. The lymph is formed by the transport of interstitial fluid surrounding the blood vessels into the lymphatic capillaries. Thus, the lipids, enzymes, and protein composition of lymph and plasma remain the same and vary only in concentrations.[1,2] The lymphatic system removes foreign bodies from the body and maintains homeostasis. Apart from mediating the immune functions and tissue fluid balance, the lymphatics also act as a reservoir for human immunodeficiency virus, filariasis, tuberculosis, and metastatic cancer cells.[3] Hence, lymphatic targeting of molecules, compounds, vaccines, and so on will be useful for diagnosis and therapy and eliciting immune responses. Colloids have emerged as an important class of drug carriers for targeted delivery into the complex lymphatic system.[4] Targeting colloids to the lymphatics involves two major steps: first, the targeting material should reach the lymphatic structures and then it should reside there for a considerable period of time by evading the host immune trafficking mechanisms. A plethora of articles on lymphatic targeting using colloids suggests that several parameters such as surface charge, particle size, molecular weight, route of administration, nature of the colloid and its surface properties (hydrophilicity and lipophilicity), and so on play a role in targeting colloids to the lymphatics, and a discussion on each of those factors is out of focus of this perspective as it would be a mere repetition of the already established facts. However, the role of phagocytosis and polyethylene glycol (PEG) attachment to colloids (PEGylation) on lymphatic

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Special Article - Stroke Recovery and Rehabilitation

Therapeutic Efficacy and Mechanism of Action Assessment of AT_1 Blocker Telmisartan with Calcium Channel Blocker Nimodipine and Cox Inhibitor Aspirin in Global Ischemic Mice Model

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Abstract

The pathogenesis involved in the cerebral ischemia is broad and treatment approach towards single target of ischemic pathological events may not appropriate to prevent the further disease progression. Considerate and development of combination therapy for cerebral ischemia with two or more potential agents targeting different molecular events of cerebral ischemia may fetch effective therapy. Therefore, the present study is planned to assess the therapeutic efficacy of combination of AT_1 blocker telmisartan (TM) with calcium channel blocker nimodipine (NM) (or) COX inhibitor aspirin (ASP) in global ischemic mice model. Global ischemia in mice was induced by occlusion of both common carotid arteries followed by reperfusion injury, and then respective treatments were made. The therapeutic efficacy of different drug combinations was evaluated through motor and muscle co-ordination tests, cerebral blood perfusion, neurotransmitter, cytokines and brain angiotensin II peptide level measurements in brain. Gene expression study (NF-κB, GSK-3β, EAAT-2, AT_1 & AT_2) and cresyl violet, synaptophysin, GFAP staining were carried out in hippocampus region of brain to support the research findings. Results indicate that TM and NM restored the CBF, improved the muscle and motor co-ordination, attenuated glutamate, aspartate and GABA release and EAAT2 expression. Further TM and NM treatments regulated the release of inflammatory cytokines, GSK-3β. ASP could control only inflammatory mediators release during ischemic condition. The AT_1 receptor expression was down regulated with TM treatment. TM has shown synergistic effect with NM and with aspirin it was observed only in few parameters. Positive correlation with glutamate clearance and cytokine levels were observed. The study can be concluded that Ang II/AT_1 pathway mediated neuroprotection during ischemic reperfusion injury. TM with NM has shown better synergistic response than TM and ASP combination. NM by preventing calcium entry has shown neuroprotective activity. Cytokines and excitotoxicity are interlinked, clearance of glutamate attenuated the inflammatory mediator response and not vice versa.

Keywords: Glutamate; Interleukins; Behaviour; Stroke; GABA; GSK3β

Abbreviations

Ang II: Angiotensin II; ANOVA: Analysis of Variance; ASP: Aspirin; AT: Angiotensin Receptors; AT_1: Angiotensin II Receptor 1; AT_2: Angiotensin II Receptor 2; BBB: Blood Brain Barrier; BCCAo: Bilateral Common Carotid Artery; BSA: Bovine Serum Albumin; Ca^{2+}: Calcium; CBF: Cerebral Blood Flow; cDNA: Complementary Deoxyribonucleic Acid; CMC: Carboxy Methyl Cellulose; COX: Cyclooxygenase; DEPC: Diethylpyrocarbonate; EAA: Excitatory Amino Acid: EAAT-2: Excitatory Amino Acid Transporter- 2; ELISA: Enzyme-Linked Immunosorbent Assay; GABA: Gamma-Aminobutyric Acid; GFAP: Glial Fibrillary Acidic Protein; GSK-3β: Glycogen Synthase Kinase-3β; HPTLC: High Performance Thin Layer Chromatography; i.p: Intraperitoneal; i.v: Intravenous; IHC: Immunohistochemistry; IL: Interleukin; IR: Ischemic Reperfused; MCAo: Middle Cerebral Artery Occluded; mRNA: Messenger Ribonucleic Acid; Na^+: Sodium; NF-κB: Nuclear Factor- κB; NM: Nimodipine; NMDA: N-Methyl-D-Aspartate Receptor; PPAR-γ: Peroxisome Proliferator-Activated Receptor Gamma; PBS: Phosphate Buffered Saline; qPCR: Quantitative Polymerase Chain Reaction; ROS: Reactive Oxygen Spices; RH: Relative Humidity; RNase: Ribonuclease; RT-PCR: Real Time - Polymerase Chain Reaction; SEM: Standard Error of Mean; TLR: Toll Like Receptor; TM: Telmisartan; TNF-α: Tumor Necrosis Factor-α

Introduction

Understanding the combination therapy in the treatment of disease is required due to multiple etiology of pathogenesis. Reports indicate that in acute ischemic stroke experimental model combination of neuroprotective drugs have shown better neuroprotective activity than the individual drug treatment [1]. The pathophysiology of

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Quillaja saponin: A prospective emulsifier for the preparation of solid lipid nanoparticles

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ABSTRACT

Quillaja saponin (QS) is a non-ionic amphiphilic surfactant of natural origin. In the present study, we evaluated its potential to form solid lipid nanoparticles (SLNs) in the presence of stearic acid (SA) as a lipid carrier and imatinib mesylate (IM) as a model drug. IM loaded solid lipid nanoparticles (IMSLNs) were prepared using the hot homogenisation method. Characterisation of IMSLNs revealed that they were quasi-spherical in shape, neutrally charged and 143.5–641.9 nm in size. Haemolysis, a toxicity issue of QS was not observed in SLNs. Comparative in vitro cytotoxicity analyses performed in human breast cancer cell line MCF7 revealed that IMSLNs were more toxic than IM. On the other hand, in vitro viability studies in the RAW264.7 cell line did not show any sign of toxicity by IMSLNs. Our results indicate that QS hold great potential in nano drug delivery as an emulsifier.

1. Introduction

Applications of solid lipid nanoparticles (SLNs) have increased tremendously in recent times due to their major advantages such as biocompatibility, biodegradability, ease of preparation, potential for scale up and cost effectiveness. SLNs consist of a solid lipid core dispersed in aqueous solutions of stabilisers or surfactants at room temperature [1]. Stearic acid, palmitic acid, glyceryl behenate, etc., are the commonly used lipids; whereas, poloxamers, polysorbates, phospholipids, bile salts, sodium oleate, cremophor EL, etc. are commonly used as stabilisers in the preparation of SLNs. In this communication, we report on the efficient preparation of SLNs loaded with an anticancer drug using Quillaja saponin (QS) for the first time.

QS is a non-ionic amphiphilic surfactant extracted from the bark of *Quillaja saponaria* (Soap bark tree). QS is a glycoside (Fig. 1) with a lipophilic backbone of quillaic acid and gypsogenic acid (a triterpene aglycone), to which hydrophilic polysaccharide moieties like rhamnose, xylose, arabinose, galactose, fucose, and glucuronic acid are attached [2]. Thus, QS can perform the role of a surfactant by adsorbing at the oil and water interface to form an emulsion [3]. Despite the characterisation of the micellar properties of QS as early as 1800 AD and approval by the US Food and Drug Administration (FDA) [4], its application has not gained prominence in the pharmaceutical sector so far. In addition to its emulsifying property, QS also possesses many bioactivities (larvicidal, antitumor, antimicrobial etc.) and is used as a natural foaming agent in cosmetic products, and as an adjuvant in vaccine delivery [5–7]. Furthermore, a product based on the *Q. saponaria* bark extract is marketed under the trade name Q-Naturale and approved by FDA for use as emulsifier in beverages.

The aim of the present study was to investigate the possibility of using QS as a surfactant in the preparation of SLNs containing an anticancer drug. Briefly, we have used stearic acid (SA), an 18-carbon fatty acid as the lipid core to encapsulate imatinib mesylate (IM), a hydrophilic anticancer drug. The prepared SLNs, loaded with IM (IMSLN), were physicochemically characterised for particle size distribution, morphology, zeta potential, crystallinity, entrapment efficiency and drug release. In addition, they were analysed for in vitro haemolytic activity, cytotoxicity and viability using cell lines. Our results demonstrate that QS is an excellent stabiliser for the preparation of SLNs without any haematotoxicity.

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0927-7765/

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In vitro Screening of the Leaf Extracts from *Gardenia ternifolia* (Forest Gardenia) for their Anticancer Activity

Damien S. Tshibangu[1], Selvaraj Divakar[2], Muthiah Ramanathan[2], Govindarajan G. Syamala[2], Koto-te-Nyiwa Ngbolua[3], Virima Mudogo[1], Dorothée D. Tshilanda[1], Benjamin Z. Gbolo[3] and Pius T. Mpiana[1*]

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Authors' contributions

This work was carried out in collaboration between all authors. Authors DST, SD and MR designed the study, performed the experimental process and wrote the first draft of the manuscript. Author GGS wrote the protocol. Authors KNN, VM, DDT and PTM managed the literature searches. Author BZG identified the plant species. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aim: The aim of the study is to evaluate the cytotoxicity of the crude extracts of *Gardenia ternifolia* (Oliv.) in human prostate cancer (PC-3) and breast cancer (MCF-7) cell lines.
Study Design: Successive extractions of *Gardenia ternifolia* leaves were performed, using petroleum ether 60-80ºC, chloroform, ethyl acetate, methanol and methanol 80%. The cytotoxicity of these extracts on human breast cancer (MCF-7), prostate cancer (PC-3), and non-cancerous rat skeletal muscle (L6) cell lines were analyzed by 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) assay.
Place and Duration of Study: This work was performed at PSG College of Pharmacy, Coimbatore, India, from 01 September 2014 to 30 December 2014.

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Comparison of pre- and post-ischemic treatment of telmisartan and nimodipine combination in experimentally induced cerebral ischemia

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Time dependent intervention plays a crucial role in preventing neurodegeneration after ischemic insult. The intensity of excitotoxicity is greater in the secondary reperfusion phase (2-4 h) compared to the primary occlusion phase (2 h), which could be attributed to secondary elevation of excitatory amino acids (EAA) in cerebral ischemia. In the present study, we tried to assess the neuroprotective effects of telmisartan and nimodipine (TM-NM) combination on the secondary reperfusion phase. The drug treatments were made immediately after reperfusion and their effects were compared with pre-treatment. The neuroprotective effect was studied using middle cerebral artery occlusion (MCAo) transient ischemic model in rats. On the 7th day after reperfusion, the rats were subjected to behavioral studies. The brain was dissected out on the 9th day to measure neurobiochemical alterations and for histopathological observations. The results have shown that TM-NM (5 mg/kg) attenuated the EAA release in different brain regions with partial restoration of energy levels in secondary reperfusion phase. Similarly, it normalized the behavioral alteration and the effect was comparable to pre-ischemic treatment (2.5 mg/kg). Pre-ischemic treatment of TM-NM (2.5 mg/kg) protected the neurons from ischemic reperfusion injury by energy dependent EAA regulation. It can be concluded from the study that, even though the pre- and post-treatment of TM-NM show similar results, the post-ischemic treatment of TM-NM combination is beneficial due to better EAA control. Since hypertension is the primary risk factor for stroke, clinical incidents of stroke in hypertensive patients receiving angiotensin receptor blockers (ARBs) can be further investigated to understand the present study in the clinical situation.

Keywords: Angiotensin, Excitatory amino acids, Focal ischemia, Hypoxia, Neurodegeneration, Stroke

The pathophysiology of cerebral ischemia is multifaceted. Occlusion of major arteries reduce the cerebral blood flow and thereby result in decreased oxygen supply, glucose level, and energy metabolites like adenosine-triphosphate/nicotinamide adenine dinucleotide phosphate (ATP/NADP) in the neurons. Deprivation of micronutrients also increases the intracellular cytosolic calcium level (Ca^{2+}) and releases excitatory amino acids (EAA), toxic free-radicals, and cytokines, which may provoke degeneration of the neurons[1,2]. These events occur during the primary (2h occlusion) and secondary (reperfusion) phases of transient focal ischemia and are time dependent. Reports indicate elevation of EAA and energy deprivation (up to 72 h) in the brain promotes the neuronal death[3]. However, results have shown greater neuronal death during the maturation of secondary reperfusion phases at 2-3 h following multiple transient forebrain ischemia[4,5]. Similarly, significant increase in glutamate, aspartate, and γ-aminobutyric acid (GABA) levels were observed compared to the initial phase (30 min) of transient ischemia in animals[5]. Even though both the phases exhibit excitotoxicity, the additional excitotoxicity after reperfusion plays an important role in ischemia[6].

Currently, in stroke therapeutics thrombolytic agents have been administered within 4 h after ischemic injury to improve cerebral blood flow and to prevent neuronal loss. In pre-clinical studies, pre-treatment with non-hypotensive dose of telmisartan (TM) (5 mg/kg) suppressed cerebral injury in a murine model of transient focal ischemia through blockade of central angiotensin receptor-1 (AT_1)[7]. Voltage dependent Ca^{2+} channel blocker nimodipine (NM) (5 mg/kg) has exhibited neuroprotection on post-ischemic administration in rats. This effect was attributed to the prevention of Ca^{2+}dependent EAA release and partial restoration of ATP/NADP levels[8]. Recently, we have reported that pre-ischemic

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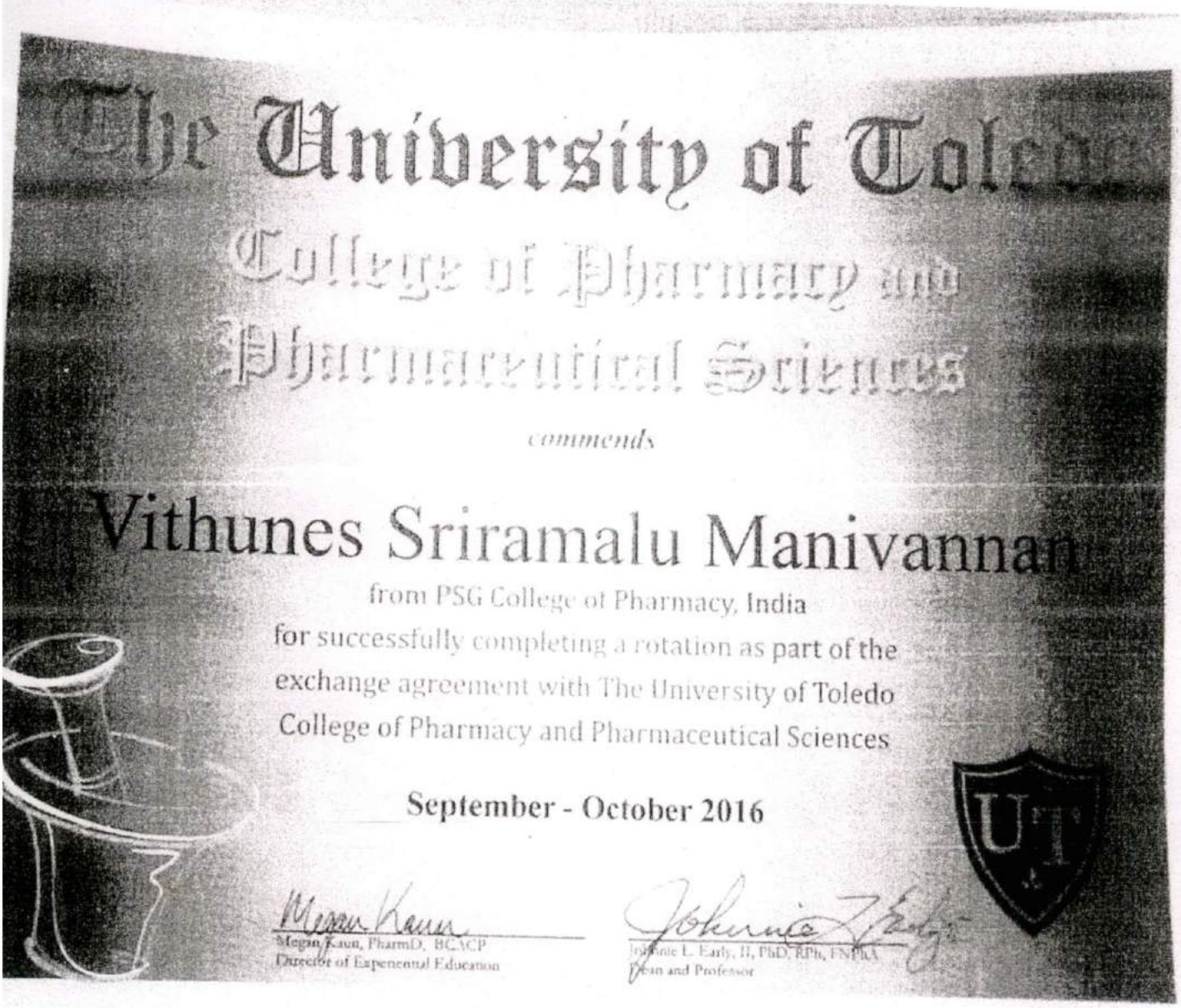
The University of Toledo
College of Pharmacy and
Pharmaceutical Sciences
commends
Vithunes Sriramalu Manivannan
from PSG College of Pharmacy, India
for successfully completing a rotation as part of the
exchange agreement with The University of Toledo
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September - October 2016
Megan Kaun, PharmD, BCACP
Director of Experiential Education
Johnnie L. Early, II, PhD, RPh, FNPhA
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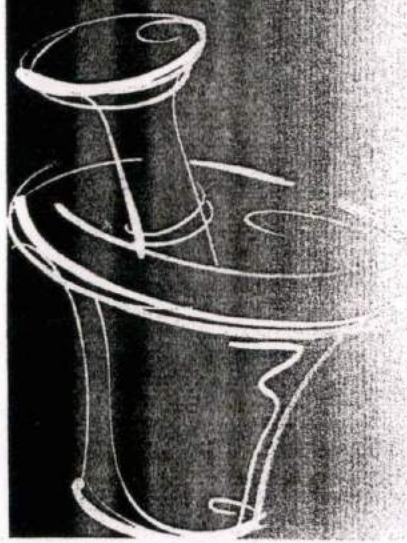

Megan Kaun

Megan Kaun, PharmD, BCACP
Director of Experiential Education

Johnnie L. Early, II, PhD, RPh, FNPhA
Dean and Professor

Design, synthesis and biological evaluation of 2-(4-phenylthiazol-2-yl) isoindoline-1,3-dione derivatives as anti-prostate cancer agents

K. Saravanan, R. Elancheran, S. Divakar, S. Athavan Alias Anand, M. Ramanathan, Jibon Kotoky, N.K. Lokanath, S. Kabilan

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Design, synthesis and biological evaluation of 2-(4-phenylthiazol-2-yl) isoindoline-1,3-dione derivatives as anti-prostate cancer agents

K. Saravanan[a], R. Elancheran[b], S. Divakar[c], S. Athavan Alias Anand[a], M. Ramanathan[c], Jibon Kotoky[b], N. K. Lokanath[d], S. Kabilan[a, *]

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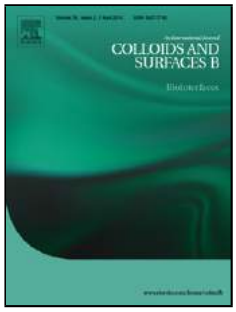
Abstract

The structural modification and molecular docking-based screening approaches on thiazole-based isoindolinediones were imposed to find the novel 2-(4-phenylthiazol-2-yl) isoindoline-1,3-dione derivatives. The best fit compounds (**6a-n**) were synthesized and evaluated their antiproliferative activities on the prostate cancer cell lines (PC-3 & LNCaP). Among them, the compound, **6m** exhibited good activity, particularly on LNCaP (IC_{50} = 5.96 ± 1.6 µM), moderately active against PC-3 cell lines as compared to bicalutamide. The compound, **6m** decreased the androgen-mediated transcription of ARE-mRNA in PSA, TMPRSS2, c-myc and cyclin D1 than R-bicalutamide. The compounds, **6e** and **6f** were reconfirmed through single crystal XRD analysis. The ADME profiling of the test compounds was evaluated to find the drug-likeness and pharmacokinetic parameters. These findings may provide vital information for the development of anti-prostate cancer agents.

Accepted Manuscript



Title: Bioadhesive micelles of D-α-tocopherol polyethylene glycol succinate 1000: synergism of chitosan and transferrin in targeted drug delivery

Authors: Poornima Agrawal, Sonali, Rahul Pratap Singh, Gunjan Sharma, Abhishesh K. Mehata, Sanjay Singh, Chellapa V. Rajesh, Bajarangprasad L. Pandey, Biplob Koch, Madaswamy S. Muthu

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Bioadhesive micelles of D-α-tocopherol polyethylene glycol succinate 1000: synergism of chitosan and transferrin in targeted drug delivery

Poornima Agrawal [b], Sonali [b], Rahul Pratap Singh [b], Gunjan Sharma [c], Abhishesh K. Mehata [a], Sanjay Singh [a], Chellapa V. Rajesh [d], Bajarangprasad L. Pandey [b], Biplob Koch [c*], Madaswamy S. Muthu [a,b*]

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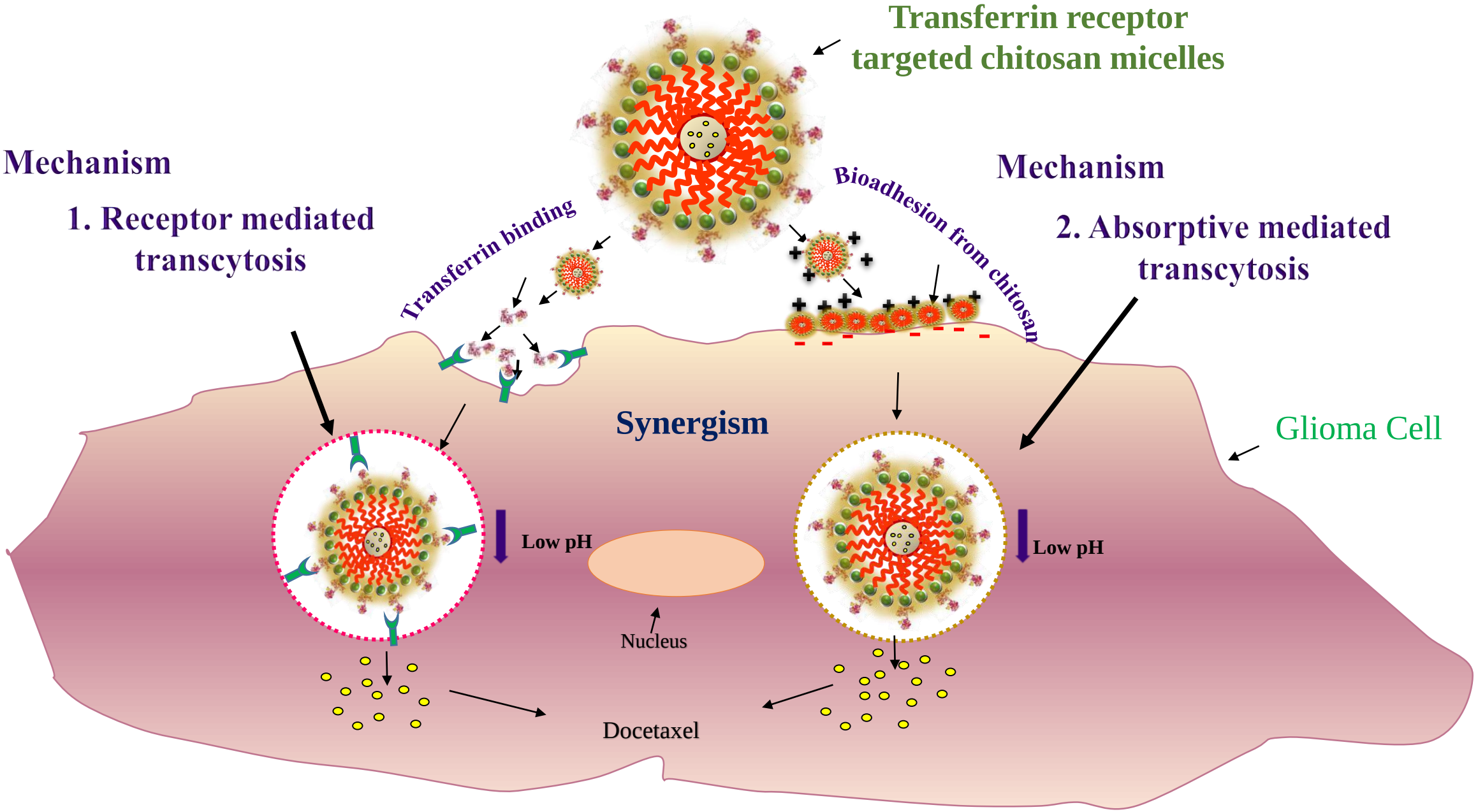
Graphical abstract



Synergistic uptake mechanisms of transferrin receptor targeted chitosan micelles

Highlights

- Developed synergistic bioadhesive micelles for brain targeted drug therapy.
- TPGS-chitosan/transferrin were synthesized and confirmed by various spectroscopic techniques.
- Cellular uptake, time-dependent bioadhesive studies and cytotoxicity of micelles were performed.
- Pharmacokinetics studies were performed for micelles in rats.
- Synergistic effect of micelles has enhanced the delivery of DTX into brain cancer cells.

ABSTRACT

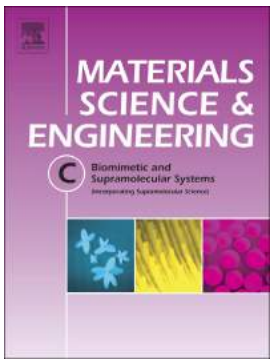
The aim of this work was to prepare targeted bioadhesive D-α- tocopheryl glycol succinate 1000 (TPGS) micelles containing docetaxel (DTX) for brain targeted cancer therapy. Considering the unique bioadhesive feature of chitosan, herein, we have developed a synergistic transferrin receptor targeted bioadhesive micelles using TPGS conjugated chitosan (TPGS-chitosan), which target the overexpressed transferrin receptors of glioma cells for brain cancer therapy. The micelles were prepared by the solvent casting method and characterized for their particle size, polydispersity, zeta-potential, surface morphology, drug encapsulation efficiency, and *in-vitro* release. The IC_{50} values demonstrated transferrin receptor targeted TPGS-chitosan micelles could be 248 folds more effective than Docel^{TM} after 24 h treatment with the C6 glioma cells. Further, time dependent bioadhesive cellular uptake study indicated that a synergistic effect was achieved with the chitosan and transferrin in targeted TPGS-chitosan micelles through the biodhesive

property of chitosan as well as transferrin receptor mediated endocytosis. The *in-vivo* pharmacokinetic results demonstrated that relative bioavailability of non-targeted and targeted micelles were 2.89 and 4.08 times more effective than Docel^{TM} after 48 h of treatments, respectively.

Keywords: Brain cancer, Targeted nanomedicines, Synergistic effect, Chitosan, Transferrin, Bioadhesive study

1. Introduction

Gliomas, astrocytomas and ependymomas are some of the types of brain tumors which are difficult to treat. Glioma is the most commonly diagnosed one, accounting for approximately 45-50% of all primary brain tumors [1]. It is an aggressive malignant form of cancer arising from neuroglial cells. Glioma often results in death of affected patients within one to two years following diagnosis. Malignant glioma can not be treated only with surgery and radiotherapy, therefore chemotherapy is recommended. But, limitations of treatment of such brain tumors arises firstly from the blood brain barrier (BBB). It is an endothelial cell monolayer combined with pericytes and astrocytes which allows only hydrophobic molecules with molecular weight usually less than 400, it blocks over 98% small molecule drugs and almost 100% large-molecule drugs such as recombinant proteins and monoclonal antibodies into the brain. Secondly, it is difficult to maintain the therapeutic levels of anticancer agent in brain tumors [2-4]. In the case of brain targeted delivery, molecules translocation across the BBB can be enhanced through covalent conjugation with polycation molecules, such as chitosan or polyethyleneimine. Also, many other



TPGS-chitosan cross-linked targeted nanoparticles for effective brain cancer therapy

Poornima Agrawal, Rahul Pratap Singh, Sonali, Laksmi Kumari, Gunjan Sharma, Biplob Koch, Chellapa V. Rajesh, Abhishesh K. Mehata, Sanjay Singh, Bajarangprasad L. Pandey, Madaswamy S. Muthu

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TPGS-chitosan cross-linked targeted nanoparticles for effective brain cancer therapy

Poornima Agrawal [b], Rahul Pratap Singh [b], Sonali [b], Laksmi Kumari [a] , Gunjan Sharma [c], Biplob Koch [c], Chellapa V. Rajesh [d], Abhishesh K. Mehata [a], Sanjay Singh [a], Bajarangprasad L. Pandey [b], Madaswamy S. Muthu [a, b*]

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Highlights

- Fabricated synergistic bioadhesive nanoparticles for brain targeted drug delivery
- TPGS-chitosan were synthesized and confirmed by FTIR, NMR and MALDI-TOF
- Cellular uptake and cytotoxicity of the nanoparticles were performed
- Pharmacokinetics was performed to study the bioavailability of the formulations
- Synergistic effect of nanoparticles has enhanced the delivery of docetaxel into brain cancer cells

TPGS-chitosan cross-linked targeted nanoparticles for brain cancer therapy

ABSTRACT

Brain cancer, up-regulated with transferrin receptor led to concept of transferrin receptor targeted anticancer therapeutics. Docetaxel loaded D-α-tocopherol polyethylene glycol succinate 1000 conjugated chitosan (TPGS-chitosan) nanoparticles were prepared with or without transferrin decoration. *In-vitro* experiments using C6 glioma cells showed that docetaxel loaded chitosan nanoparticles, non-targeted and transferrin receptor targeted TPGS-chitosan nanoparticles have enhanced the cellular uptake and cytotoxicity. The IC_{50} values of non-targeted and transferrin receptor targeted nanoparticles from cytotoxic assay were found to be 27 and 148 folds higher than Docel^{TM}. *In-vivo* pharmacokinetic study showed 3.23 and 4.10 folds enhancement in relative bioavailability of docetaxel for non-targeted and transferrin receptor targeted nanoparticles, respectively than Docel^{TM}. The results have demonstrated that transferrin receptor targeted nanoparticles could enhance the cellular internalization and cytotoxicity of docetaxel via transferrin receptor with improved pharmacokinetics for clinical applications.

Keywords: Brain cancer, Transferrin receptor, Targeted nanomedicines, Synergistic effect, Chitosan, TPGS

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RESEARCH PAPER

A Retrospective Qualitative Study on Current Diabetic Foot Ulcer Management and Discussion on Extended Role of Clinical Pharmacist

A. Porselvi, M. S. Uma Shankar, K. S. Lakshmi, V. Sankar

ABSTRACT

Diabetic foot ulcers (DFU) are chronic complications due to poor diabetic control. Diabetic foot ulcers can lead to lifelong disability and substantially diminish the quality of life. The aim of this study was to carry out a thorough evaluation of diabetic foot ulcer management, compare current scenario of DFUs care with the International guidelines and to identify the extended roles of clinical pharmacist to improve the conditions of diabetic patient with foot ulcers.

It is a retrospective qualitative study carried out in two tertiary care hospitals of Tamil Nadu state. The patients were selected based on inclusion and exclusion criteria admitted in the hospitals with diabetic foot ulcers. The patient's socio-demographic and clinical characteristics tools from the patient medication records (PMR) were collected and taken into considerations for the study.

The study revealed that diabetic foot ulcer was more prevalent among male patients with type 2 diabetes since 11 to 25 yrs belongs to the age group between 51-60 years. It was found that 60.5% of the patients having at least one co-morbid condition and 90.6% of patients possess one or more risk factors to develop diabetic foot ulcers. Glycated hemoglobin (HbA_{1c}) test were done only by 54.7% of the patients, which showed that it was not insisted as an important identification tool for diabetic foot ulcer. The PMR revealed numerous antibiotics switch-over for the wound treatment as well.

From the study it was concluded that an immediate requirement and thorough evaluation of enhanced foot care management, patient centered care and diabetic foot surveillance etc is needed for diabetic foot ulcer management. A comparative current scenario of DFUs care with the International guidelines and its adaptation and modifications according to our need is to be emphasized. Amalgamation of clinical pharmacy services with the multidisciplinary diabetic foot care team services is to be made. The clinical pharmacist's intervention is to be put forward to improve the conditions of diabetic patient with foot ulcers to decrease the alarming incidences in Indian hospital settings.

Key Words: Diabetes, diabetic foot ulcer, wounds, guidelines, clinical pharmacy intervention

INTRODUCTION

Diabetes is a group of heterogeneous disorders characterized by hyperglycemia and glucose intolerance due to insulin deficiency, impaired effectiveness of insulin action, or both [1]. About 15%-25% of diabetic patients will develop chronic ulcers of foot or lower extremity during their lifetime [2-4].The etiology of foot ulcers is multi-factorial [3,5] among which peripheral vascular disease, neuropathy and retinopathy are considered to be the most important causative factors [6]. Foot ulcers in diabetic patient are the major sufferings and cost-effective [7]. Diabetic foot ulcer patients use more in and outpatient health resources and

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frontiers in Cellular Neuroscience

ORIGINAL RESEARCH
published: 22 March 2017
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Bioactive Fraction of *Annona reticulata* Bark (or) *Ziziphus jujuba* Root Bark along with Insulin Attenuates Painful Diabetic Neuropathy through Inhibiting NF-κB Inflammatory Cascade

Raghuram Kandimalla[1], Suvakanta Dash[2], Sanjeeb Kalita[1], Bhaswati Choudhury[1], Sandeep Malampati[3], Rajlakshmi Devi[1], Muthiah Ramanathan[4], Narayan C. Talukdar[1] and Jibon Kotoky[1,5]**

[1] Drug Discovery Laboratory, Institute of Advanced Study in Science and Technology, Guwahati, India, [2] Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati, India, [3] School of Chinese Medicine, Hong Kong Baptist University, Kowloon Tong, Hong Kong, [4] PSG College of Pharmacy, Coimbatore, India, [5] National Institute of Pharmaceutical Education and Research, Guwahati, India

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The present study explains the neuroprotective ability of bioactive fractions of *Annona reticulata* bark (ARB) and *Ziziphus jujuba* root bark (ZJ) along with insulin against diabetic neuropathy. By using different solvents of increasing polarity ARB and ZJ were undergone for bioactive guided fractionation. The neuroprotective ability of the all the plant fractions were tested against H_2O_2 induced toxicity in SHSY5Y neuroblastoma cell lines and DRG neuronal cells. Among all the fractions tested, the methanol extract of ARB and ZJ (ARBME and ZJME) and its water fractions (ARBWF and ZJWF) exhibited significant neuroprotection against H_2O_2 induced toxicity in SHSY5Y cells and DRG neuronal cells. Further both the active fractions were tested against streptozotocin (55 mg/kg i.p.) induced diabetic neuropathy in male Wistar rats. Body weight changes, blood glucose levels and pain threshold through hot plate, tail immersion, cold plate and Randall-Sillitto methods were measured throughout the study at weekly interval. After completion of the drug treatment period, all the animals were sacrificed to measure the sciatic nerve lipid peroxidation, antioxidative enzyme levels (SOD, catalase, and GSH) and cytokine levels (IL-1β, IL-6, IL-10, TNF-α, iNOS, and NFκB) through ELISA and western blotting analysis. Results of this study explain that ARBME, ZJME, ARBWF, and ZJWF along with insulin potentially attenuate the thermal, mechanical hyperalgesia and cold allodynia in diabetic neuropathic rats, where insulin treatment alone failed to diminish the same. Reduction of sciatic nerve oxidative stress, NF-κB and iNOS mediated inflammatory cascade and normalization of abnormal cytokine release confirms the possible mechanism of action. The present study confirms the neuroprotective ability of ARB and ZJ against painful diabetic neuropathy through inhibiting oxidative stress and NF-κB inflammatory cascade.

Keywords: neuro-inflammation, diabetic neuropathic pain, NF-κB, iNOS, cytokines, oxidative stress

Design, Synthesis and Biological Evaluation of Novel 1, 3- thiazolidine-2, 4-diones as Anti-prostate Cancer Agents

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Anti-Cancer Agents in Medicinal Chemistry, 2017, *17*, 1756-1768

RESEARCH ARTICLE

Design, Synthesis and Biological Evaluation of Novel 1, 3-thiazolidine-2, 4-diones as Anti-prostate Cancer Agents

Ramakrishnan Elancheran[1,2,*], Kuppusamy Saravanan[3], Selvaraj Divakar[4], Sima Kumari[1], V.Lenin Marutha-nila[1], Senthamarikannan Kabilan[3], Muthiah Ramanathan[4], Rajlakshmi Devi[1] and Jibon Kotoky[1,*]

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ARTICLE HISTORY

Received: August 16, 2016
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Abstract: ***Background*:** Androgen receptor is an attractive target for the treatment of prostate cancer. The 1,3-thiazolidine-2,4-diones possess a wide diversity of important biochemical effects and interesting pharmacological properties.

***Objective*:** The aim of the study is to find the experimental and computational methods to investigate the interference of 1,3-thiazolidine-2,4-diones with androgen receptor against prostate cancer.

***Method*:** Structural modification and molecular docking-based virtual screening approaches were imposed to identify the novel 1,3-thiazolidine-2,4-diones by using Schrödinger (Maestro 9.5). The best fit molecules (**3-12 & 23-31**) were synthesized and characterized using spectroscopic techniques, then *in vitro* antioxidant and anti-prostate cancer activities were evaluated. Further, the structure of the intermediate (**18**) was confirmed by single crystal XRD analysis. The mechanism studies were performed through the gene expression for the compounds, **29, 30**, and **31,** the standards, dihydrotestosterone and R-bicalutamide.

***Results*:** The compounds, **29, 30** and **31** showed comparatively significant antioxidant activity and better anti-proliferative activity against PC-3 and LNCaP cell lines. Also, very low cytotoxicity was observed in the non-cancerous cell (3T3). The compounds, **29, 30** and **31** significantly decreased the mRNA expression of AR-stimulated genes, PSA and TMPRSS2, which demonstrated their anti-prostate cancer activities. ADME/T properties prediction of the compounds (**3-12** and**23-31**) showed the promising drug-likeness and pharmacokinetic parameters without toxicity. Moreover, DFT calculations apparently confirmed the stable conformer of the compound, **31**.

***Conclusion*:** These findings may provide the essential information for the development of anti-prostate cancer agents.

Keywords: Androgen receptor, prostate cancer, AR antagonist, thiazolidinedione, ADME/T, synthesis.

1. INTRODUCTION

Prostate cancer (PCa) is the most often diagnosed noncutaneous tumor and the second leading cause of cancer deaths among men in the United States [1, 2]. PCa growths are primitively dependent on endogenous androgens that activate the androgen receptor (AR), a member of the nuclear receptor superfamily and play a crucial role in gene transcription, growth, and functions of the prostate as well as having effects on hair and skin. Androgen deprivation therapies are currently recommended along with radiation treatment, also after surgery or radiation if any cancer cells remain [3]. Current chemotherapeutic drugs such as abiraterone, bicalutamide, cabazitaxel, and enzalutamide have been practiced for the treatment of Castration-Resistant Prostate Cancer (CRPC) patients. Interestingly, compounds like MDV 3100, ARN-509 and ONC1-13B demonstrated strong antagonist activity in the prostate, also bind to the AR with high affinity and more potent than bicalutamide. In addition, AR gene mutation, such as T877A and W741C/L is an important mechanism for castration-resistance and remains the major challenge in the clinical studies [4]. Most of the antiandrogens are derived from flutamide (1a), bicalutamide (1b), Enzalutamide (1c), nilutamide (1d), DDL-02 (1e), DDL-03 (1f), N-(4-(4-hydroxyphenoxy)-3-methylphenyl)benzamide (1g), (Z)-5-(4-propoxybenzylidene) thiazolidine-2,4-dione (1h), (Z)-5-(3-(trifluoromethyl)benzylidene) thiazolidine-2,4-dione (1i), and OSU-CG12 (1j) bearing a 4-cyano or 4-nitro-N-substituted (3-trifluoromethyl) phenyl or (3-trifluoromethyl) phenyl group (Fig. **1**) [3, 5]. Recently, Enzalutamide (MDV3100) has been the FDA approved drug that has been reported to be more effective than bicalutamide and could solve the problems to some extent [3, 6]. Therefore, the modification of existing drugs and evolution of specific targeted therapeutics are currently carried out to minimize the toxicity, minimizing drug resistance and lowering therapeutic doses. In a previous study, we have reported the design and synthesis of several oxobenzimidazoles and thiazinones that demonstrated the relevant cytotoxicity and pharmacokinetic properties [5, 7]. There are several studies reported that five-membered heterocyclic compounds play an important role in the development of anti-cancer drugs, where 1,3-thiazolidine-2,4-diones have been reported to be a potential scaffold and have therapeutic importance when combined with aromatic rings through exocyclic double bond produce a wide range of biological activities such as anti-diabetic, anti-inflammatory, anti-oxidant, anti-tubercular, anti-microbial, anti-convulsant and cytotoxic activities [8-11].

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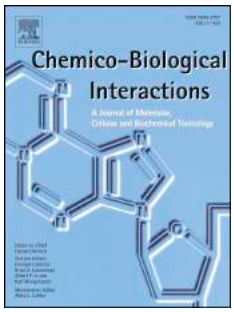

Iminoenamine based novel androgen receptor antagonist exhibited anti-prostate cancer activity in androgen independent prostate cancer cells through inhibition of AKT pathway

S. Divakar, K. Saravanan, P. Karthikeyan, R. Elencheran, S. Kabilan, K.K. Balasubramanian, Rajlakshmi Devi, J. Kotoky, M. Ramanathan

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Iminoenamine based novel androgen receptor antagonist exhibited anti-prostate cancer activity in androgen independent prostate cancer cells through inhibition of AKT pathway

S. Divakar[a], K. Saravanan[b], P. Karthikeyan[c], R. Elencheran[e], S. Kabilan[b], K. K. Balasubramanian[c, f], Rajlakshmi Devi[d], J. Kotoky[e], M. Ramanathan[a],*

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Abstract

Treatment by androgen receptor (AR) antagonists is one of the regimens for prostate cancer. The prolonged treatment with AR antagonist leads to the expression of point mutation in the ligand binding domain of the AR. This point mutation causes resistance to AR

Indian Academy of Sciences
Bengaluru

Indian National Science Academy
New Delhi

The National Academy of Sciences, India
Allahabad

SUMMER RESEARCH FELLOWSHIP PROGRAMME

CERTIFICATE

This is to certify that Mr N Balaji worked on a project entitled "Development and biomedical application of green synthesis based nanoformulation against H1N1 virus" during September–November 2017 as a Summer Research Fellow under the supervision of Dr Ganesh Chandra Sahoo, Rajendra Memorial Research Institute of Medical Sciences, Patna. The Summer Research Fellowship Programme is jointly sponsored by IASc (Bengaluru), INSA (New Delhi) and NASI (Allahabad).

K L Sebastian

Place: Bengaluru
Date: 08-01-2018

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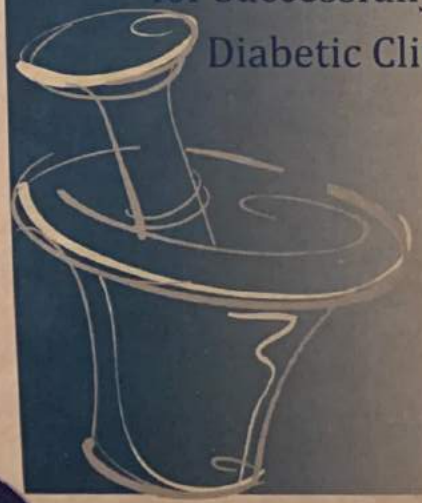

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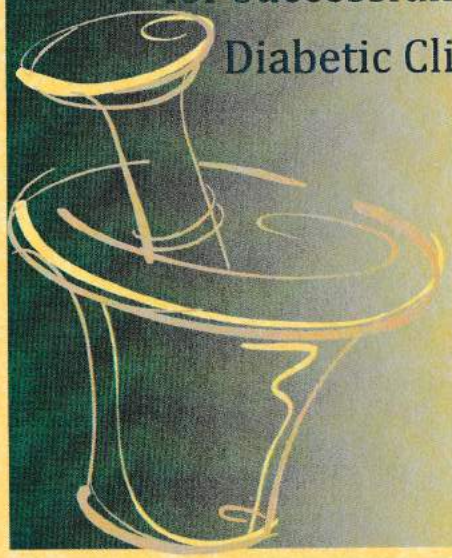

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June 9, 2017

CERTIFICATE-2

BRNS Ref.: Concept Proposal No 9.1.2

This is to certify that the Project Entitled "**Carboplatin Immobilised Metallic Nanoparticles for Targeted delivery to Ovarian Cancer Cells**" submitted for financial support to the Board of Research in Nuclear Sciences (BRNS) by Dr. V. Sankar, PSG College of Pharmacy, Coimbatore as Principal Investigator (PI), has been formulated in consultation with me. I have gone through the application (Project Proposal Application: PPA), which is as per the current BRNS format.

The project would be executed in active collaboration between us and I shall ensure for timely submission of yearly progress reports and financial documents towards conclusion of the project as scheduled

This proposal had been approved by the Chemistry and Isotope Group Board as a concept proposal.

P. A. Hassan
(Principal Collaborator)

Date: 09-06-2017

Place: Mumbai

डॉ. पी. ए. हसन/Dr. P. A. HASSAN
अध्यक्ष, तापीय एवं अंतरापृष्ठीय रसायनिकी अनुभाग
Head, Thermal & Interfacial Chemistry Section
रसायन प्रभाग / Chemistry Division
भाभा परमाणु अनुसंधान केंद्र / Bhabha Atomic Research Centre
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Signature of Executive Authority of "PSG College of Pharmacy" a Unit under PSG & Sons' Charities" with stamp

Dr.M.Ramanathan, M.Pharm,Ph.D
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4

Date: 13.09.2017

Prof. Sundara Ramaprabhu
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Date:

Dr. V Sankar
Principal Investigator
Date: 13/09/2017

PSG COLLEGE OF PHARMACY
PEELAMEDU
COIMBATORE-641 004.

Dr. Muthiah Ramanathan
Co-Investigator
Date: 13.09.2017

Dr.M.Ramanathan, M.Pharm,Ph.D
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4.

Signature & Seal of all co-investigators, project investigators, and executive authorities of participating institutions is compulsory

Part 6: DECLARATION/CERTIFICATION

It is certified that

1. The research work proposed in the scheme/project entitled **"Development of Natural Polymer Based Thermal In Situ Nanogel To Cross Blood- Retinal Barrier For Diabetic Retinopathy"** does not in any way duplicate the work already done or being carried out elsewhere on the subject.
2. The same project proposal has not been submitted to any other agency for financial support.
3. The emoluments proposed for the manpower are as admissible to persons of corresponding status employed in the institute/university or as per the Ministry of Science & Technology guidelines.
4. Necessary provision for the scheme/project will be made in the Institute/ University/ Organization budget in anticipation of the sanction of the scheme/ project.
5. If the project involves the utilization of genetically engineered organisms, we agree to submit an application through our Institutional Bio-safety Committee. We also declare that while conducting experiments, the Bio-safety Guidelines of the Department of Biotechnology would be followed into.
6. If the project involves field trials/experiments/exchange of specimens, etc. we will ensure that ethical clearances would be taken from concerned ethical Committees/ competent authorities and the same would be conveyed to the Department of Biotechnology before implementing the project.
7. If the Project requires any statutory permission(s) for any authority to carry out the project, the same would be obtained and intimated to DBT before taking up research activities.
8. It is agreed that any research outcome or intellectual property rights(s) on the invention(s) arising out of the project shall be taken in accordance with the instructions issued by Department of Biotechnology, Govt. Of India.
9. We agree to accept the terms and conditions of Department of Biotechnology, Govt. Of India.
10. The institute/university agrees that the equipment, other basic facilities and such other administrative facilities as per terms and conditions of the grant will be extended to investigator(s) throughout the duration of the project.
11. The Principal Investigator(s) involved in the project has sufficient service duration to carry out the project. In case his tenure get expire before completion of project necessary provision would be made to allow him to complete the project for its logical conclusion.
12. The Institute assumes to undertake the financial and other management responsibilities of the project.
13. The details & information given in the Project proposal are true & factual.

Signature of Executive Authority of "INDIAN INSTITUTE OF TECHNOLOGY, MADRAS" with stamp

प्रो. कृष्णन बालसुब्रमणियन
Prof. KRISHNAN BALASUBRAMANIAN
डीन / DEAN
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Date: 12.09.2017

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Principal
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Peelamedu, Coimbatore-4.

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Website : www.psgpharma.ac.in

MEMORANDUM OF UNDERSTANDING (MoU)

The memorandum of understanding is entered for providing the following services between

PSG College of Pharmacy, Coimbatore, having its registered office at Peelamedu, Coimbatore - 641004 herein referred to as the "FIRST PARTY"

AND

PSGR Krishnammal College for Women, Coimbatore, having its registered office at Peelamedu, Coimbatore-641004 herein referred to as the "SECOND PARTY"

NOW IT IS HEREBY AGREED BY AND BETWEEN THE PARTIES HERETO:

Preamble:

Institutional collaboration Initiatives will lead to efficient complementation of resources of both the sponsors eventually leading to the development of a house of excellence for quality training, research and development which will be of immense mutual benefit and relevant to societal benefit. Realizing this objective, the colleges, named above, have signed this MoU in order to achieve the desired results for the benefit of the students and community.

Whereas the first party is willing to give internship training program and project work to research scholars and UG and PG students **of second party**

TERMS AND AGREEMENT

1. The institution to support in internship training and research projects.
2. This is a non-exclusive agreement and is effective from the year 2017 onwards.
3. For the services rendered by one party to other, the service charges, if applicable, shall be mutually agreed upon, and paid to the service provider.
4. The MoU shall be in force for a period of THREE years and can be terminated with three months notice on either side.
5. This agreement is governed by and construed in accordance with Indian Law.

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Website : www.psgpharma.ac.in

6. The Head of the Department of Botany will be the Coordinator for the interaction on behalf of the second party and The Principal will be the Coordinator for the interaction on behalf of the first party.

The first party and **the second party**, each represent that, it has read and understood this agreement, that by signing below it agrees to be bound by its terms, and that it has caused this Agreement be executed by its authorized representatives.

Place: Coimbatore - 4
Date: 11.12.2017

Signature of the first party

Dr. M. Ramanathan
Principal
PSG College of Pharmacy
Peelamedu
Coimbatore – 641004

Dr. M. Ramanathan, M.Pharm, Ph.D.
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4.

Signature of the second party

Dr. S. N. Padma Devi
HOD, Dept of Botany
PSGR Krishnammal College for Women
Peelamedu, Coimbatore – 641004

Dr. S. N. PADMA DEVI, M.Sc., M.Phil., B.Ed., Ph.D.
Head of the Department of Botany
PSG & R. Krishnammal College for Women
Peelamedu, Coimbatore - 641 004.

Witnesses:

Dr. V. Sankar
Vice Principal
PSG College of Pharmacy
Peelamedu
Coimbatore – 641004

PSG COLLEGE OF PHARMACY PEELAMEDU COIMBATORE-641 004.

Dr. S. Nirmala
Principal
PSGR Krishnammal College for Women
Peelamedu, Coimbatore – 641004

PRINCIPAL
PSGR KRISHNAMMAL COLLEGE FOR WOMEN
COIMBATORE - 641 004.

P.S.G. R. KRISHNAMMAL COLLEGE FOR WOMEN COIMBATORE-641 004.

NATIONAL INSTITUTE OF MENTAL HEALTH & NEUROSCIENCES
(INSTITUTE OF NATIONAL IMPORTANCE) BENGALURU - 560 029

NIMH:A&E:TM:TRG-PSY:2017/1149 Date: 21.11.2017

The Assistant Professor
Department of Psychiatry
PSG Institute of Medical Sciences & Research
Coimbatore – 641 004

Sir/Madam,

Sub: Request for Permission to come as observer at this institute – reg.
Ref: Your letter dated 10.11.2017

* * * * *

With reference to the above, I am directed to convey the permission of the Competent Authority for the student/students of your Institution to come as **observer** at this Institution as follows:

1	Number of Observer	01
2	Name of Observer	Mr.Alan Kurian
3	Department at which Observership permitted	Psychiatry
4	Date & Duration of Observership **No change of date will be entertained**	02.12.2017 to 31.12.2017
5	Training fee	Rs.3000/- per month or part thereof

- The observer should compulsorily carry their college ID cards while posted at NIMHANS.
- One stamp size photo should be given at the time of joining for issue of temporary ID card. (ID card should be returned at the end of training without fail)
- Observer should carry a copy of this letter without fail.
  The Observer fee for the whole duration of observership has to be paid by Debit/Credit Card on the day of joining. The observer fee once paid will not be refunded.

I am also directed to inform you that the visiting students/trainees should make their own arrangement for accommodation. However all efforts will be made to provide hostel accommodation, but this will be subject to availability as on the date of joining and on payment of charges as below:-

1. Hostel Rent: Rs.100/- per day	**2. Caution Money Deposit:** Rs.1000/- (refundable)

Allotments, payment, check-outs, refunds and other official transactions are possible only on working days between 10 am and 3 pm. **Accommodation will not be provided to the candidates coming earlier than the scheduled date of training.**

On arrival, the observer must contact the undersigned for further needful.

Yours faithfully

ADMINISTRATIVE OFFICER (A&E)
Administrative Officer (A & E)
National Institute of Mental Health & Neuro Sciences, Bangalore-560 029.

Copy to: The HOD of Psychiatry, NIMHANS

From,

Alan kurian

11PD003

Pharm.D (Intern)

Psg college of pharmacy

Peelamedu, Coimbatore .

Tamil Nadu.

Through,

Dr. Prudence A Rodrigues

Professor and Head,

Department of Pharmacy Practice,

PSG College of Pharmacy.

To,

Dr. M. Ramanathan

Principal

PSG College Of Pharmacy

Peelamedu ,Combatore.

Subject: regarding permission to attend training in NIMHANS Hospital under the department of psychiatry for 1 month.

Respected Sir,

I would like to get trained in NIMHANS Hospital, Bangalore under the department of Psychiatry from December 1st to Dec.31st with the aim of acquiring comprehensive clinical knowledge, where clinical pharmacists can contribute significantly towards better therapeutic outcomes among psychiatric population which is least explored currently in India.

I kindly request your permission to grant me this period with OD & I assure to hold high the fame & reputation of my institution.

Yours sincerely,

Coimbatore

30-10-17.

Alan kurian

HONEY BEE NETWORK

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December 9 - 29, 2017

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Certification of Participation

This is to certify that Mr./Ms. **Janani P** has participated in BIIS for validation, value addition and product development around grassroots innovations. He/she has contributed earnestly on the project entitled **Anti-dysentery and phytochemical studies of the mixture of *Mangifera indica*, *Phyllanthus emblica* & *Syzygium cumini*.** We hope that he/she will continue to support and cooperate with Honey Bee network and SRISTI in blending formal and informal science and technology for empowering grassroots innovators.

Prof. Anil K Gupta
Coordinator, SRISTI, Ahmedabad

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Certification of Participation

This is to certify that Mr./Ms. **Eldhose Jose** has participated in BIIS for validation, value addition and product development around grassroots innovations. He/she has contributed earnestly on the project entitled **Evaluation of growth-inhibition effect of *Nerium indicum* L. leaves extract on insect suspension cell culture of *Spodoptura litura*.** We hope that he/she will continue to support and cooperate with Honey Bee network and SRISTI in blending formal and informal science and technology for empowering grassroots innovators.

Prof. Anil K Gupta
Coordinator, SRISTI, Ahmedabad

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Journal homepage: http://scienceq.org/Journals/JABZ.php
Short Communication Open Access

Medicinal Plants from Democratic Republic of the Congo as Sources of Anticancer Drugs

Koto-te-Nyiwa Ngbolua[1,2,*], Damien S. Tshibangu[2], Pius T. Mpiana[2], Virima Mudogo[2], Dorothée D. Tshilanda[2], Colette Masengo Ashande[1], Selvaraj Divakar[3], Muthiah Ramanathan[3], Govindarajan Syamala[3]

[1]University of Gbadolite, P.O. Box 111 Gbadolite, Nord-Ubangi Province, Democratic Republic of the Congo

[2]Faculty of Science, University of Kinshasa, P.O. Box 190 Kinshasa XI, Democratic Republic of the Congo

[3]Department of Pharmacology, PSG College of Pharmacy, Coimbatore, India

*Corresponding author: Koto-te-Nyiwa Ngbolua, Ph: +243 81 68 79 527, E-mail: jpngbolua@unikin.ac.cd

Received: December 02, 2017, Accepted: January 14, 2018, Published: January 14, 2018.

ABSTRACT:

According to the WHO, more than 80% of the population in Africa resort to the traditional medicine for their health care. In the present study, a survey was carried out among traditional practitioners and the most cited plant species was submitted to anticancer experiments *in vitro*. The results revealed that *Gardenia ternifolia* contains secondary metabolites with anticancer activity and is selective towards breast (MCF-7) cancerous cell lines.

Keyword: *Evidence based Medicine, indigenous knowledge, botanical Medicine, cancer, DR Congo.*

INTRODUCTION

Cancer is a major public health problem all over the world and constitutes the second leading cause of death after cardiovascular disease [1]. Because of serious side effects of both chemo-and radiation therapies, many patients seek alternative and complementary methods of treatment. Several anti-cancer agents derived from plant species (Taxol, Camptothecin, Topotecan, etc. and their derivatives) are in clinical use or in preclinical development (Flavopiridol, Silvestrol, Betulinic acid, etc.) [2].

Democratic Republic of the Congo (DRC) as one of the hotspots of plant biodiversity in the world could play a key role in the R & D of new anti-cancer agents from it flora [3]. The aims of this multidisciplinary research program were:(a)To validate scientifically the traditional use of selected plant species by investigating anti-cancer activity of their extracts as a possible source of anti-cancer hits using human prostate (PC-3) and breast (MCF-7) cancerous cell lines and non-cancerous rat skeletal muscle L6 cell lines as model systems (Scientific evidence based Traditional Medicine); (b)To evaluate the therapeutic index of the biologically active extracts; (c)To develop anti-cancer phytomedicines as a result of the transformation of indigenous/ethno-medical knowledge into large scale action by the mean of Science and Technology(Research for sustainable development).

MATERIALS AND METHODS

An ethno-botanical survey was conducted in DRC according to the principles laid out in the Declaration of Helsinki and the Nagoya protocol. Traditional Healers and/or medicinal plant vendors (50) were interviewed about medicinal plants used in Congolese folk medicine [4]. The powdered leaves of Gardenia ternifolia were extracted by maceration. Successive extractions were carried out with organic solvents of increasing polarity (Petroleum ether, Chloroform, Ethyl acetate, Methanol and Methanol 80%). Anti-cancer bioactivity of different extracts was assessed by MTT assay. Paclitaxel was used as positive control [5].

RESULTS AND DISCUSSION

Ethno-botanical survey revealed that the most cited plant species was Gardenia ternifolia (or Lembanzau in Kikongo) with a high value of informant consensus factor (0.361). Biological screening revealed that chloroform and ethyl acetate soluble fractions are biologically active against MCF-7 cell lines with a CC50 (50% cytotoxic concentration) of 21.62±1.6µg/mL and 45.44±2.2µg/mL respectively. For PC-3 cell lines, the CC50 were 9.66±2.6µg/ml and24.47±1.1µg/ml, respectively for chloroform and ethyl acetate extracts. The petroleum ether, methanol and methanol 80% crude extracts were inactive against both MCF-7 and PC-3 cell lines (50 < CC50<100 or CC50> 100 µg/ml).The chloroform extract displayed interesting therapeutic index or safety ratio (CC50 L6/CC50 MCF-7 or PC-3 ≥3).This extract is 3 or 7 times selective in killing the cancerous cell lines (MCF-7 or PC-3) than the non-cancerous cell lines (L6) [5]. This could be due to the different secondary metabolites extracted with the chloroform solvent.

Figure 1 : *Gardenia ternifolia*

HONEY BEE NETWORK

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Biotech Innovation Ignition School (BIIS)

February 5 - 26, 2018

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Certification of Participation

This is to certify that Ms. **Sharmilaa D.** has participated in BIIS for validation, value addition and product development around grassroots innovations. She has contributed earnestly on the project entitled **Anti microbial, anti oxidative and anti inflammatory activities of *Heracleum candicans* against UTI.** We hope that she will continue to support and cooperate with Honey Bee network and SRISTI in blending formal and informal science and technology for empowering grassroots innovators.

Prof. Anil K Gupta
Coordinator, SRISTI, Ahmedabad

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Gmail principal cp <principalpsgcp@gmail.com>

Collagen formulation development

2 messages

principal cp <principalpsgcp@gmail.com> 12 April 2018 at 17:04
To: SUBASH CHANDRA BOSE SANTHOSH KUMAR <santhospillai@gmail.com>
Cc: sivavega <sivavega@gmail.com>

Dear Dr. Santhosh,

We are in receipt of your email dated 4th April 2018, related to collagen formulation development to treat wounds. The work has been allotted to Dr. V. Sankar and Dr. V. Sivakumar. They go through the questions, by Monday we will send back to you details. If any further clarifications required, I will call you back.

We can also plan one brainstorming session to develop full length project, so that the end of the project we can come out with product. We can also explore the financial support from Govt agencies.

Looking forward to hear from you on this.

I also copied this mail to Dr. V. Sivakumar.

--

Principal
PSG College of Pharmacy
Peelamedu, Coimbatore
Tamilnadu 641004 India
www.psgpharma.ac.in
+91 422 434 5841

Santhospillai <santhospillai@gmail.com> 12 April 2018 at 17:21
To: principal cp <principalpsgcp@gmail.com>
Cc: sivavega <sivavega@gmail.com>

Thank you ,after getting answers we will do brainstorm ,we will proceed further
[Quoted text hidden]
--

in fb tw G+

With respect + encouragement

S.SanthoshPillai | Director | 9361894618

Sales & marketing | Nvron Life science Ltd

Gmail

principal cp <principalpsgcp@gmail.com>

(no subject)

2 messages

principal cp <principalpsgcp@gmail.com>
To: SUBASH CHANDRA BOSE SANTHOSH KUMAR <santhospillai@gmail.com> 25 April 2018 at 16:50

Dear Mr. Santhosh,

I have sent you the details of the questions related to Collagen. We also discussed with the physician Dr. Aruchamy. The out come of the survey are encouraging. The output of the collagen products can be narrow down. Next week 3rd or 4th May if you can come over here, we can discuss the details and plan for the next level of development.

--
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore
Tamilnadu 641004 India
www.psgpharma.ac.in
+91 422 434 5841

Collagen based products survey.doc
28K

Santhospillai <santhospillai@gmail.com>
To: principal cp <principalpsgcp@gmail.com> 26 April 2018 at 11:30

Dear sir ,

Excellent work ,it gives lot of clarity , as per your communication i will meet soon
[Quoted text hidden]
--

in fb tw G+

With respect + encouragement

S.SanthoshPillai I Director I 9361894618

Sales & marketing I Nvron Life science Ltd

02-05-2018, 12:58 PM

Collagen based products survey – Answers

1.Why do you prefer collagen?
ANS: Burn management to avoid fluid loss

2.When do you prefer collagen?
ANS: 1st, 2nd degree burn

3.Any prefer brand?
ANS: Kollagen

4.Why do you prefer it over other brands? (format, cost, effectiveness, imported quality any other issues like adhesion to wound etc.,)
ANS: format, cost, effectiveness, quality

5.What feature do you wish collagen product to have in future? (format, application time, method of application, adhesion, packging etc,)
ANS: Application time

6.Any physical attribute of the collagen dressing product you like or dislike most?
ANS: Both equal

7.How well/ strongly collagen adhere to wounds?
ANS: only superficial adhesion to bed, discharge wound not adhere

8.Is it desirable to adhere to wounds?
ANS: Not always

9.What do you think is best about collagen dressing product over other product?
ANS: Not clear

10.How frequently you change collagen dressing in burn, chronic wounds?
ANS: 5days, 3days

11.Do you apply collagen on infected wounds? If not why?
ANS: No – aggravate infection spread of infection

12.what do you wish if collagen is to be applied on infected wounds?
ANS: Not to apply

13.Will it be better if collagen is in the form of paste or cream?
ANS: No

14.Will it be better if collagen is in the form of foam?
ANS: No

15.will it be better if collagen is dry sheet?
ANS: No

16.Do you prefer a transparent/translucent collagen sheet over an opaque one?

ANS: Translucent

17.Do you feel collagen prevent oxygen to a deep wound?
ANS: Deep wound no effect

18.Do you think collagen has the healing capacity independent of any drugs formulated with it?
ANS: No

19.Do you think collagen reduces pain?
ANS: Yes

20.What do you think are limitations of collagen based dressing ? like applicability in case of emergencies, onsite solution, third degree wound.
ANS: Onsite solution, third degree wound

21.When do you use hydrogel for dressing?
ANS: Not used

22.Any ECM product are you aware of?
ANS: Not used

23.What is your preferred dressing product for seriously infected wound?
ANS: Saline dressing, Antibiotics

24.How often it needs to be changed /exäminined as routine?
ANS: 5 days, 3 days

25.Do you find collagen dressing helpful in case of venous ulcers?
ANS: No

26.Do you find collagen dressing helpful in arterial ulcers?
ANS: No

27.Do you find collagen dressing helpful in diabetic wounds?
ANS: No

28.Do you find collagen dressing useful in case of bed sores
ANS: No

Discussion and survey outcome on this topic:

1. Innovative product can be made in the form of translucent collagen sheet/ cream with quick application time .

2. For treating Arterial ulcer , Diabetic wounds , third degree burns collagen loaded antibiotics can be tried because scientific literature supports the use of collagen for this conditions .

3. Collagen works by increasing the movement of keratinocytes and fibroblasts, skin cells that are vital in tissue regrowth. By expediting new skin development, collagen can

help reduce the risk of infection, giving bacteria less time to move in and infect your bloodstream.

4. Collagen has the capacity of healing wounds independent of any drugs formulated with it along with reduction of pain ..

Indian Academy of Sciences
Bengaluru

Indian National Science Academy
New Delhi

The National Academy of Sciences, India
Allahabad

SUMMER RESEARCH FELLOWSHIP PROGRAMME

CERTIFICATE

This is to certify that Mr S Arvinth Kumar worked on a project entitled "Design, synthesis & cloning of synthetic guide RNA for genomic engineering" during May - July 2018 as a Summer Research Fellow under the supervision of Dr Sivaprakash Ramalingam, Institute of Genomics & Integrative Biology, Delhi. The Summer Research Fellowship Programme is jointly sponsored by IASc (Bengaluru), INSA (New Delhi) and NASI (Allahabad).

M.R.N. Murthy

Place: Bengaluru
Date: 08-08-2018

M.R.N. Murthy
Chairman, Science Education Panel

INDIAN ACADEMY OF SCIENCES
P.B. No. 8005, C.V. Raman Avenue, Sadashivanagar P.O., Bengaluru 560 080, India
Email: sumfel@ias.ernet.in

THE UNIVERSITY OF TOLEDO
1872

June 21, 2018

Dr. V.Sankar, Professor and Head
Department of Pharmaceutics Vice principal, PSG college of pharmacy, Peelamedu,
Coimbatore 641004, Tamilnadu, India

Dear Dr. Sankar,

Subject: Letter of acceptance from host scientist at the University Toledo

I am writing to offer a letter of acceptance of the research plan titled "Synthesis Characterization and Evaluation of Folic acid Conjugated Gemcitabine Silver Nanoparticle coated with pH Stimuli Polymer on Breast Cancer Cell lines".I am delighted at the opportunity to collaborate with you in this research project. **Hereby I am giving my consent to take the research scholar Mr. Arjun Karuppaiah at PSG college of Pharmacy for one year in the Pharmaceutics lab under the DST – Overseas Visiting Doctoral Fellowship**. I look forward to your success in pursuing this grant application.

Sincerely,

Jerry Nesamony, Ph.D.

Associate Professor (Pharmaceutics)

University of Toledo

College of Pharmacy and Pharmaceutical Sciences
Pharmacy Practice • Mail Stop 1013 • 3000 Arlington Ave. • Toledo, OH 43614
Phone: 419.383.1951 • Fax: 419.383.1950 • www.utoledo.edu

THE UNIVERSITY OF TOLEDO
1872

June 21, 2018

Dr. V. Sankar, Professor and Head
Department of Pharmaceutics Vice-Principal
PSG College of Pharmacy
Peelamedu, Coimbatore 641004, Tamilnadu, India

Dear Dr. Sankar,

Please accept this letter of acceptance of the research plan titled "Synthesis Characterization and Evaluation of Folic acid Conjugated Gemcitabine Silver Nanoparticle coated with pH Stimuli Polymer on Breast Cancer Cell lines" which involves Dr. Jerry Nesamony. I am pleased to see this project under development as it helps our collective fulfillment of a portion of the memorandum of understanding between our Colleges. And of, I am in enthusiastic support of the project.

Please keep me informed on the success of the application, and the project.
With kind regards, I remain.

Very truly yours,

Johnnie L. Early, II, PhD, RPh, NPhA Fellow
Dean and Professor
JLE/ct

College of Pharmacy and Pharmaceutical Sciences
Office of the Dean • Mail Stop 1013 • 3000 Arlington Ave. • Toledo, OH 43614
Phone: 419.383.1997 • Fax: 419.383.1907 • www.utoledo.edu/pharmacy

SAMFORD UNIVERSITY
McWHORTER SCHOOL OF PHARMACY
Birmingham, Alabama USA

Certifies That

Sheryl Elizabeth Jess

has successfully completed the

"International Pharmacy Scholars Program"

June 20 - June 29, 2018

Michael A. Crouch, Pharm.D., BCPS, FASHP,
Fred E. McWhorter Dean and Professor
Samford University, McWhorter School of Pharmacy

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Peelamedu, Coimbatore-641004

23.08.2018

Certificate

With high regards, we are certifying that **Dr. G. Syamala, Associate Professor**, Department of Pharmacognosy, PSG College of Pharmacy, Peelamedu, Coimbatore, has been an invited as an external faculty to deliver lecture for II B. Sc Botany students regarding Job oriented course entitled "Pharmaceutical Sciences" organized in the Department of Botany, PSGR Krishnammal College for Women, Coimbatore. She has delivered lectures on the following dates

1st, 2nd, 14th, & 23rd of August 2018- (2 hrs/day)

Looking forward for further collaborative activities

Signature

JOC Co-ordinator

(Dr. M. Kamalam)

Dr. N. Kamalam, M.Sc., M.Phil., Ph.D.
Associate Professor
Department of Botany
PSGR Krishnammal College for Women
Peelamedu, Coimbatore - 641 004.

Head of the Department

(Dr. C. Krishnaveni)

Dr. C. KRISHNAVENI
M.Sc., M.Phil., B.Ed., Ph.D.
Head of the Department of Botany
PSGR Krishnammal College for Women
Peelamedu, Coimbatore - 641 004.

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Peelamedu, Coimbatore-641004

31.07.2018

Certificate

With high regards, we are certifying that **Mrs. S. Vanitha, Assistant Professor**, Department of Pharmacognosy, PSG College of Pharmacy, Peelamedu, Coimbatore, has been an invited as an external faculty to deliver lecture for II B. Sc Botany students regarding Job oriented course entitled "Pharmaceutical Sciences" organized in the Department of Botany, PSGR Krishnammal College for Women, Coimbatore. She has delivered lectures on the following dates.

24th, 25th, 26th & 31st of July 2018 (2 hrs/day)

Looking forward for further collaborative activities

Signature

JOC Co-ordinator
Dr. M. Kamalam
Dr. N. Kamalam, M.Sc., M.Phil., Ph.D.
Associate Professor
Department of Botany
PSGR Krishnammal College for Women
Peelamedu, Coimbatore - 641 004.

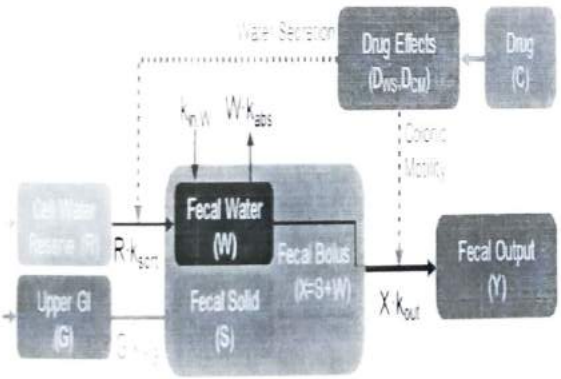
Head of the Department
Dr. C. Krishnaveni
Dr. C. KRISHNAVENI
M.Sc., M.Phil., B.Ed., Ph.D.
Head of the Department of Botany
P.S.G.R. Krishnammal College for Women
Peelamedu, Coimbatore - 641 004.

Translational Research Group, DMPK, Takeda Pharmaceuticals, San Diego, CA, USA; [2]Gastroenterology Drug Discovery Unit, Takeda Pharmaceuticals, San Diego, CA, USA.

Introduction/Objective: Pre-clinical animal models for gastrointestinal (GI) motility diseases (e.g. constipation, diarrhea) play an important role in drug discovery but are challenging to interpret and translate. Rodent models are commonly used, as they provide a system where fecal production and consistency can be measured. Measurements of fecal pellet output (FPO) and water content are frequently assumed to be correlated with colonic motility and water secretion, respectively. Physiologically, however, colonic motility and water secretion effects on FPO are not independent, which can lead to incorrect interpretation drug's mechanism of action based on FPO study data. Whole GI transit time data along with water secretion measurements from a colonic loop study provide additional information that can explain drug's mechanism of action. However, it is not always clear how endpoints from different studies fit together. A mathematical model provides a quantitative framework to evaluate multiple measurements comprehensively and to effectively assess drug's mechanism of action.

Methods and Results: Here, we derive a pharmacokinetic/pharmacodynamic (PKPD) model of rodent FPO that integrates the mechanisms of water secretion and colonic motility. Parameter sensitivity analysis suggests that both water secretion and colonic motility influence fecal output and consistency, which makes FPO study endpoints problematic for identification of mechanism of action. We further show that rodent colon size can confound assessment of drug's effect on colonic motility and suggest an update to the study design that, in concert with the PKPD model, can eliminate this mischaracterization. Finally, we validate the model by fitting it to colonic loop and FPO data for a known clinical compound, recapitulating the compound's effects on GI transit time.

Conclusions: These analyses illustrate that a mechanistically-derived PKPD model is essential to properly characterize GI physiology and pharmacology, as well as a drug's mechanism of action, for ultimate translation of pre-clinical rodent data to human.



Figure

T-013

Using Mechanistic Modeling to quantify ADC-anti-VEGF combination antitumor response: Impact of tumor vasculature changes on ADC tumor targeting

Jared Weddell, Manoj Chiney, Mohamad Shebley, John P. Gibbs

Clinical Pharmacology and Pharmacometrics, AbbVie Inc., North Chicago, IL, USA

Objectives: Antibody drug conjugates (ADCs) promise selective tumor targeting of potent small molecule agents. Anti-VEGF combination therapy has potential to improve drug tumor penetration and antitumor response[1]. The objective was to use a mechanistic modeling based approach to quantify effect of anti-VEGF therapy on ADC tumor biodistribution and tumor volume reduction (TVR) using T-DM1-bevacizumab combination as a case study.

Methods: A mechanistic model platform comprising (1) minimal PBPK model, (2) Krogh cylinder model, and (3) mechanistic TVR model was verified using clinical data for T-DM1, at the approved dose of 3.6 mg/kg Q3W, in metastatic breast cancer patients using MATLAB®. The biological effect of bevacizumab, at a clinical dose of 15 mg/kg Q3W, on tumor vasculature was captured using the Krogh cylinder model through changes in parameters pertaining to capillary density, interstitial fluid pressure, permeability, and tumor perfusion. The model did not incorporate independent bevacizumab effects on TVR.

Results: The ADC model met performance criteria in capturing T-DM1 monotherapy pharmacokinetics and objective response rate. For T-DM1-bevacizumab combination therapy, the model predicted that there is 14% greater TVR at 6 months than T-DM1 monotherapy. While combination and T-DM1 monotherapy equally killed tumor cells near the capillary, the combination therapy increased spatial T-DM1 tumor distribution, which resulted in 38% increased cell death farthest from the capillary. For hypothetical scenarios evaluated, there was significant impact of the choice of bevacizumab and T-DM1 dose on the predicted TVR for the combination.

Conclusions: Simulations based on a mechanistic ADC modeling platform predicted improved ADC tumor biodistribution with anti-VEGF combination therapy, relative to ADC monotherapy. Application of such mechanistic modeling approaches, by exploring hypothetical scenarios, can provide valuable insights into drug development strategies for combination therapies.

Funding: AbbVie provided financial support for the studies and participated in the design, study conduct, analysis, and interpretation of data as well as the writing, review, and approval of abstract.

Conflict of Interest: All authors are employees of AbbVie, Inc. and may hold stock or stock options.

Reference

1. Cesca (2015) *Mol Cancer Ther* 15:125.

T-014

Development of a model to predict lean liver volume (*LLV*) for use in scaling drug clearance

Jaydeep Sinha[1], Stephen Duffull[1], Bruce Green[2], T. Ponnuswamy[3], B. Devanand[3], M. Ramanathan[4], S. Ramalingam[3], Hesham Al-Sallami[1]

[1]Otago Pharmacometrics Group, School of Pharmacy, University of Otago, Dunedin, New Zealand; [2]Model Answers R&D Pty Ltd, Brisbane, Australia; [3]PSG Institute of Medical Sciences and Research, Coimbatore, India; [4]PSG College of Pharmacy, Coimbatore, India

Objectives: For hepatically-cleared drugs, clearance (*CL*) is known to correlate with liver size [1]. Theoretically, the lean portion of the liver (lean liver volume, *LLV*) is the metabolically active part of the liver and may be a better scaler of *CL* than total liver volume. The aim of this work was to develop a model for *LLV* from readily-measurable patient variables.

Methods: *LLV* data (single measurement) were derived by subtracting the liver fat from the total liver volume, measured by computed tomography in 100 adult Indian participants [2]. A model for *LLV* was developed using NONMEM v7.3 and the following covariates: weight (*WT*), fat free mass (*FFM*), *SEX*, clinical chemistry, and liver and kidney function markers. Model selection was performed using likelihood ratio test. Initially, allometric scaling of body size and composition covariates (*WT* and *FFM*) was done by estimating the population *LLV* (θ_{LLV}) and exponent (θ_{exp}) with and without the addition of *SEX*, then other variables were tested using stepwise covariate modelling (SCM). The final model was evaluated using visual predictive checks and non-parametric bootstrap analysis.

Results: The only significant covariates were *WT*, *FFM* and *SEX*. *WT* was statistically preferred to *FFM* but was indistinguishable from the combination of *FFM* and *SEX*. However, a subgroup analysis of the overweight and obese patients indicated a preference for *FFM* and *SEX*. The θ_{LLV} estimates were 1440 (95% CI: 1381–1499) and 1280 (95% CI: 1187–1373) mL for male and female participants respectively. The θ_{exp} estimate of FFM was 1.01 (95% CI: 0.80 to 1.20).

Conclusions: A model to predict *LLV* from *SEX* and *FFM* was developed and evaluated. The model could be considered as a potential scaler of individual drug dosage.

Encore: The results in this abstract have been previously presented in part at [PAGANZ 2018, Melbourne, Australia 6–7th Feb, 2018] and published in the conference proceedings as abstract.

References

1. Murry et al. Drug metabolism and disposition. 1995;23(10).
2. McLeay et al. Open Obesity Journal. 2014;6(1).

T-015

A Quantitative Systems Pharmacology Model of Glucose-Insulin Regulation to Guide the Design and Evaluation of Novel Basal Insulins with Optimal Risk–Benefit Profile

Jeanne Geiser, Parag Garhyan, Jenny Chien

Eli Lilly and Company, Indianapolis, IN, USA

Objectives: To evaluate the effects of differential hepatic to peripheral tissue distributions of basal insulins using a Quantitative Systems Pharmacology (QSP) model with glucose-insulin regulation and metabolism (endogenous glucose production [EGP], glucose disposal rate [GDR]), hypoglycemic risk and subsequent glycemic control in patients with type 1 diabetes (T1DM) and type 2 diabetes (T2DM).

Methods: A QSP model of glucose regulation was developed previously[1]. Basal insulins with similar pharmacokinetic profiles but different tissue distribution properties were evaluated in the model, ranging from balanced hepatic to peripheral activity ratio, to primarily hepatic acting or primarily peripherally acting. Two 26 week parallel-arm studies in T1DM and T2DM (insulin-naive or on basal insulin) populations were simulated to compare these basal insulins in terms of glucose, HbA1c, and hypoglycemic rates. Insulin dose titration followed the modified Riddle algorithm [2] with compliance ranging from 70 to 90%.

Results: Simulations show an expected difference in EGP and GDR based on tissue distributions. Trial simulations show that, following treatment to basal insulins with different tissue distributions, different ratio of hepatic to peripheral activity led to different HbA1c reduction and hypoglycemia rates. The basal insulin with greater peripheral action achieved less HbA1c reduction, but with higher incidence of hypoglycemia, compared to a hepatically active and peripherally restricted basal insulin in both T1DM and T2DM.

Conclusions: A QSP model with physiological parameters is a valuable research tool to aid in the understanding of the mechanisms of action and alternative dosing strategy for a novel insulin. A basal insulin with attenuated peripheral activity relative to liver may provide optimal risk–benefit profile over existing basal insulins.

References

1. Kumar R, et al., J Pharmacokinet Pharmacodyn (2014) 41(suppl 1): M-028.
2. Riddle MC, et al., Diabetes Care (2003) 26: 3080–3086.

T-016

Integration of Population Exposure–Response and Physiological Based Pharmacokinetics Modeling Approaches to Evaluate Gastric-Emptying Induced Drug Interaction Risks for Dulaglutide

Lai-San Tham[1], Karen B Schneck[2], Jeanne S Geiser[2], Maria Posada[2] and Gemma Dickinson[2]

[1]Lilly Centre for Clinical Pharmacology, Singapore;
[2]Eli Lilly and Company, Indianapolis

Objectives: Use an integrated population exposure–response (ER) and physiologic-based pharmacokinetics (PBPK) modeling approach to assess the impact of delayed gastric emptying (GE) from a single 4.5 mg subcutaneous (SC) dose of dulaglutide on the systemic exposures of coadministered oral medications (acetaminophen, digoxin, lisinopril, metformin and s-warfarin).

Methods: Acetaminophen and dulaglutide PK data were fitted using nonlinear mixed effects modeling (NONMEM version 7.3.0). The effect of dulaglutide was introduced as a delay on acetaminophen's GE rate constant from the stomach to small intestine. A ratio of the time for 50% of acetaminophen to remain in the stomach with and without dulaglutide coadministration (R_{T50}) was derived. Separate dose–response curves for R_{T50} were constructed over the weekly SC dulaglutide dose ranges 0.05 mg to 8 mg in type 2 diabetics and 1 to 3 mg in healthy subjects. Model predictions of dulaglutide and acetaminophen PK were then qualified against historical data. Next, PBPK models for acetaminophen, digoxin, lisinopril, metformin and s-warfarin from the Simcyp software (version 16) were implemented to derive their respective maximum exposures (C_{max}) and area under concentration–time curve (AUC) with and without 1.5 mg dulaglutide. Each PK model was qualified with observed Cmax and AUC values from historical drug–drug interaction studies. Finally, the R_{T50} for a 4.5 mg dulaglutide dose was introduced to the mean GE time of each qualified model to predict the C_{max} and AUC of these medications when coadministered with 4.5 mg dulaglutide.

Results: The integrated ER/PBPK approach simulated dulaglutide 4.5 mg lowered C_{max} for some coadministered oral agents with geometric mean ratios between 0.53 to 0.96; AUC ratios were between 0.76 to 1.00 (Table 1). These ratios were within the PK parameter variabilities of the coadministered medications

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Research paper

Design, synthesis and biological evaluation of 2-(phenoxymethyl)-5-phenyl-1,3,4-oxadiazole derivatives as anti-breast cancer agents

K. Lakshmithendral [a], K. Saravanan [a], R. Elancheran [a], K. Archana [a], N. Manikandan [b], H.A. Arjun [a], M. Ramanathan [b], N.K. Lokanath [c], S. Kabilan [a, *]

[a] Drug Discovery Lab, Department of Chemistry, Annamalai University, Annamalai Nagar, 608002, Tamil Nadu, India
[b] Department of Pharmacology, PSG College of Pharmacy, Coimbatore, 641004, Tamil Nadu, India
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ARTICLE INFO

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Keywords:
Estrogen receptor
Breast cancer
1,3,4-Oxadiazoles
Molecular docking

ABSTRACT

Structural based molecular docking approach revealed the findings of 2-(phenoxymethyl) -5-phenyl-1,3,4-oxadiazole derivatives. The compounds (**7a-o**) were synthesized and characterized well by using conventional methods. The compounds, **7b** and **7m** were reconfirmed through single crystal XRD analysis. The synthesized compounds (**7a-o**) were evaluated their antiproliferative activities against MCF-7 and MDA-MB-453. Furthermore, Lipinski's rule of five and pharmacokinetic properties were predicted for the test compounds. These results demonstrate that the compounds **7b** and **7d** exhibit more potent cytotoxicity and **7d** exhibits dose-dependent activity and reduced cell viability. Further, the mechanism of action for the induced apoptosis was observed through morphological changes and western blotting analysis. These findings may furnish the lead for further development.

1. Introduction

Cancer is a group of heterogeneous diseases involving dysregulation of cell growth and functions to proliferate to other parts of the body. Breast cancer (BCa) is the second most common cancer worldwide. National Cancer Institute (NCI) has assessed that the diagnosis of 266,120 new cases and 40,920 dying due to BCa in the United States in 2018 [1,2]. The global burden of BCa surpasses all other cancers, and the frequency is still rising. Over the last decade, several drugs and monoclonal antibodies have been approved and are in the advanced stages of clinical trials that target the receptors and signaling pathways [3]. ER-positive (ER+) breast cancer is estrogen-dependent including luminal types A and B. ER-negative (ER-) breast cancer is estrogen independent including the subtypes human epidermal growth factor receptor 2 (HER2) in which ErbB2 is overexpressed [3]. Tamoxifen is a non-steroidal antiestrogen and widely used for the treatment of breast cancer, which acts on estrogen receptor [4]. Inhibition of cancerous inhibitor of protein phosphatase 2A (CIP2A) determines the effects of tamoxifen-induced apoptosis in ER-negative breast cancer cells [5]. ER alpha, ER beta, and Progesterone receptor are not expressed in Triple-negative breast cancer (TNBC) which still exhibits an extraordinary clinical challenge due to the unavoidably ineluctable advancement of medical obstruction [6]. DNMT3B (DNA Methyltransferase 3 Beta) is a Protein-Coding gene, which is related to abnormal methylation of tumour suppressor and repair genes and its overexpression contributes to oncogenic processes and tumorigenesis [7]. OTUD1 (ovarian tumour deubiquitinase 1) represses breast cancer metastasis by mitigating Transforming growth factor beta (TGF-β) induced pro-oncogenic responses via deubiquitination of SMAD7 (SMAD Family Member 7) which is a protein-coding gene [8]. The five-membered heterocyclic compound containing more than two heteroatoms like azole, thiazole, oxadiazole, triazene, imidazole, purines, etc. have tremendous importance in human life due to their assortment of medicinal applications against several maladies [9,10].

In recent years, the structural activity relationship with target structures and their mechanism used for the drug design and oxadiazole has been reported with various biological activities such as antitubercular, antiviral, antifungal, antibacterial, antimicrobial, antidiabetic and anticancer activities [11–14]. In particular, 1,3,4-oxadiazole is an important moiety that exhibits more potent and selective inhibitory activity against various cancer cell lines.

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0223-5234/

Collaborative project
2019 ICMR.

Detailed proposal submission for funding under "Extramural Adhoc" Scheme in ICMR

FORMAT OF RESEARCH PLAN

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1. **Title of the proposed research project:**

   Brain targeted delivery of telmisartan and nimodipine loaded intranasal solid lipid nanoparticles *in situ* gel for cerebral ischemia

2. **Summary (up to 250 words):**

Background: Repurposing the existing clinical agents for other disease conditions are emerging because it holds promising benefits by lowering cost and time required in routine drug development process. In our earlier studies, we have demonstrated the repurposing benefits of telmisartan and nimodipine (anti-hypertensive drugs) combination in cerebral ischemic rats **(Justin et al., 2014, Ramanathan & Justin, 2016)**. In continuation, it is advantageous to develop as novel formulation for above combination at minimal dose may further scale-up its clinical application in cerebral ischemia.

Novelty: This is a first nanoformulation approach using the above combination with novel releasing pattern of drugs. Treatment for cerebral ischemia is time dependent, earlier treatment through intra nasal route could save the degeneration of millions of neurons.

Objective: To develop the telmisartan and nimodipine loaded intranasal solid lipid nanoparticles (TM-NM-SLNs) *in situ* gel for the treatment of cerebral ischemia

Methods: The TM-NM-SLNs will be prepared by homogenization coupled with ultra-probe sonication method using glyceryl monostearate and palmitic acid (tripalmitin-TP) as lipids and polysorbate 80 as surfactant. After pharmaceutical characterization, it will be loaded into poloxamer 407 based *in situ* gel with carbopol 974 P. The gelation properties, *In-vitro* cytotoxicity, cellular uptake efficiency, brain imaging, nasal mucosal toxicity, pharmacokinetics assessments followed by neuroprotective evaluation using ischemic animal models will be carried out.

Expected outcome: TM-NM-SLNs *in situ* gel could be a potential nanoformualtion for the treatment of cerebral ischemia which could prevent the further degeneration of neurons. This formulation can be implemented in the therapeutic practice for the cerebral ischemia after clinical evaluation.

3. **Keywords: (maximum 6)**

   Combination therapy, Solid lipid nanoparticles, Intranasal *in situ* gel, Brain targeting, Rapid cum sustained delivery, Ischemic stroke

DECLARATION AND ATTESTATION

i. I/We have read the terms and conditions for ICMR Research Grant. All necessary Institutional facilities will be provided if the research project is approved for financial assistance.

ii. I/We agree to submit within one month from the date of termination of the project the final report and a list of articles, both expendable and non-expendable, left on the closure of the project.

iii. I/We agree to submit audited statement of accounts duly audited by the auditors as stipulated by the ICMR.

iv. It is certified that the equipment(s) is/are not available in the Institute/Department or these are available but cannot be spared for the project

v. It is further certified that the equipment(s) required for the project have not been purchased from the funds provided by ICMR for another project(s) in the Institute.

vi. I/We agree to submit (online) all the raw data (along with descriptions) generated from the project to the ICMR Data Repository within one month from the date of completion /termination of the project.

If any equipment already exists with the Department/Institute, the investigator should justify purchase of the another equipment.

Signature of the:

a) Principal Investigator : **Dr. A. Justin**

Dr. A. Justin, M.Pharm., Ph.D.,
Assistant Professor, Dept.of Pharmacology
JSS College of Pharmacy, Ootacamund - 643 001.
The Nilgiris, Tamilnadu

b) Co-Investigator 1 : **Dr. N. Jawahar**

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JSS College of Pharmacy
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Mobile No: 9486946314

Co-Investigator 2 : **Dr. V. Sankar** 23/02/19

Dr. V. Sankar, M.Pharm., Ph.
Professor & Head,
Department of Pharmaceutics, Vice Pri
PSG College of Pharmacy
Peelamedu, Coimbatore - 641004.
E.Mail: sansunv@yahoo.co.in
Mobile No: 98422 90701

Co-Investigator 3 : **Dr. James Chelliah**

Dr. James P.C. Chelliah
Assistant Professor (Faculty Fellow)
Neuroscience Unit
Jawaharlal Nehru Centre for Advanced
Scientific Research,
Jakkur, Bangalore - 560 064.
Karnataka, India.

c) Head of the Department

Head
Dept. of Pharmacology
JSS College of Pharmacy
Rocklands, Ooty - 643 001
Tamil Nadu, India

Signature of the Head of the Institution with seal

PRINCIPAL
J. S. S. College, of Pharmacy
Rockland's Ootacamund-643001

Date: 23.02.2019

Received on 12-3-19 at 9.30 AM

PSG COLLEGE OF PHARMACY

(An ISO 9001 : 2008 Certified Institution)

ACCREDITED WITH 'B' GRADE BY NAAC (1st CYCLE)

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11.03.2019

Dr. M. Ramanathan, M. Pharm, Ph.D.,
Principal

To
NVR Associates Ltd,
1st Floor, 2E/6, Moti Bhawan
Jhandewalan Extn
New Delhi - 55

Dear Sir,

Please find herein attached signed MOU for undertaking a research assignment, to carry out enumeration of district hospitals, multi-speciality hospitals and medical colleges across Coimbatore district of Tamil Nadu State. The GST declaration and PAN/Account details also enclosed for your reference.

Thanking you,

Yours truly,

Dr. M. Ramanathan
Principal

Dr. M. Ramanathan, M.Pharm, Ph.D.
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4.

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PSG.

8.2.19

MEMORANDUM OF UNDERSTANDING [MOU]

Between

NVR & Associates Limited

&

PSG College of Pharmacy

This documents constitutes an agreement between **NVR & Associates Limited [CIN: U74899DL2000PLC105032]**, a company incorporated under the Companies Act 1956/sole proprietary concern/partnership firm, having its registered office at 2E/6, Moti Bhawan Jhandewalan Extension New Delhi -110055

And

PSG College of Pharmacy, a unit under PSG & Sons' Charities, a charitable trust having its registered office at Avinashi Road, Peelamedu, Coimbatore - 641004, hereinafter referred to as PSG College of Pharmacy;

Scope of Services

Undertake a research assignment, to carry out enumeration (detailed survey) of all district hospitals, multi-specialty hospitals and medical colleges as per the tools provided, across Coimbatore district of Tamil Nadu state. The total expected number of hospitals to be covered is 270 in the above-mentioned district. The PSG will appoint a Supervisor and a set of students/enumerators for 3 months duration to carry out the research.

General Terms of MOU

To carry out the data collection the service provider/Supplier will provide the following manpower

A. NVR

(a) Facilitate training to the team (of students & supervisor) identified by the institution for 2-4 days
(b) Provide printed (hard) copies of the Enumeration Block maps
(c) Provide the list of hospitals to be covered in the district of Coimbatore of Tamil Nadu state (270 Hospitals)
(d) Provide printed (hard) copies of the questionnaires or tablets with pre-loaded application
(e) Appoint a local representative for monitoring the research assignment and providing any required support
(f) Support with all required authorization documents (for the institute to approach the establishments and carry out survey)
(g) Share a reporting structure and format

B. PSG College of Pharmacy

(a) Appoint a Principal Investigator or Supervisor to plan, manage and monitor the research assignment. He or she would serve as a Single Point of Contact for the research assignment
(b) Select a team of students to participate in the Research Assignment and allocate locations for carrying out the survey
(c) Devise a quality control mechanism, such as accompaniment with students (for at least 10% of the establishments covered), to ensure standard protocols being maintained
(d) Carry out resource enumeration of all the available hospitals, district hospitals and medical colleges for the identified districts.
(e) Ensure that the scanned copy of collected data is sent to the NVR.
(f) Ensure high standard of accuracy and confidentiality is maintained during collection of data
(g) Coordinate with quality check team (at National level) regarding any discrepancy in quality of the data collected at the field level & take appropriate corrective measure as suggested and required.
(h) Prepare and submit a report on the assignment within 10 days after the end of the data collection and quality assessment

Terms and Conditions

(a.) The Service Provider is not allowed to carry out any other research along with assigned research work.
(b.) All equipment, instruments and materials used by Service Provider in connection with performance of the Research shall at all times remain under the sole control and ownership of NVR. The Service Provider will need to return all the filled-in questionnaires or tablets (and any other material as may be shared) to NVR in proper, undamaged condition, upon completion of the data collection process
(c.) IQVIA (client of NVR) shall retain ownership of all data and information generated to use the data for internal and commercial purposes
(d.) Without the prior written consent of IQVIA, the Service Provider will not publish any data or results of the survey carried out in the form of articles / journals / thesis / dissertations, or otherwise of their own choosing, methods, information or to present at international, national or regional professional meetings or symposia conducted in connection with this research assignment.
(e.) NVR recognizes the involvement of Service Provider in the Research and will acknowledge the names of Principal Investigator / Supervisor, Students and the name of the University/College when published or otherwise available for public dissemination. A certificate will be issued to each of the participating members from the Service Provider's end, from IQVIA.
(f.) Neither NVR or the Service Provider will be considered to be in default if delays in or failure of performance shall be due to uncontrollable forces the effect of which, by the exercise of reasonable diligence, the nonperforming party could not avoid. It includes, fire, flood, earthquakes, storms, lightning, epidemic, war, riot, civil disturbance, sabotage, inability to procure

permits, licenses, or authorizations from any state, local, or federal agency or person for any of the supplies, materials, accesses, or services required to be provided by either Sponsor.

(g.) CONFIDENTIAL RELATIONSHIP

a. Confidentiality - During the Term of this Agreement the Service Provider/Supplier or its employees or agents may learn or acquire certain NVR information. Service Provider/Supplier shall treat all such information, including this Agreement, as confidential, whether or not so labeled or identified, and shall not disclose any part thereof without the prior written consent of NVR. This clause shall survive the termination of this Agreement.

b. Employees and Agents - Service Provider/Supplier shall disclose NVR's confidential information to its employees or agents who are under obligations of confidentiality on a need-to-know basis only. Service Provider/Supplier shall secure confidentiality agreements from all of its employees and agents to whom NVR's information is disclosed.

c. Return of Materials upon Termination – Forthwith upon expiration or termination of this Agreement, the Service Provider/Supplier shall (a) deliver (or at NVR's option, destroy) to NVR the original and all copies of all confidential information, including but not limited to all diagrams, designs, schematics, and work in progress in the Service Provider/Supplier's possession or control and (b) delete all NVR confidential information the Service Provider/Supplier's computers, systems, storage apparatuses, and any other media. Upon request, Service Provider/Supplier shall deliver to NVR a certificate signed by an authorized officer of Service Provider/Supplier which certifies that Service Provider/Supplier has complied fully with the obligations of this Section.

(h.) INTELLECTUAL PROPERTY RIGHTS

a. The Service Provider/Supplier acknowledges that all works of authorship performed under this Agreement are subject to NVR's direction and control and that such works constitute a work for hire. All proprietary information developed, created, invented, devised, conceived or discovered by Receiving Party that are subject to copyright are explicitly considered by to be "works made for hire" and shall remain the sole property of NVR. The Service Provider/Supplier agrees to assign, transfer, and convey all rights, title and interest in and to any copyrightable or patentable inventions, processes, improvements, ideas, copyrightable works of art, trademarks, copyrights, formulae, manufacturing technology, developments, writings, discoveries, and trade secrets that it may make, conceive, or reduce to practice, from the effective date of this Agreement, if intellectual property was developed or performed solely for NVR using the NVR's resources/information. This clause shall not apply of such Intellectual Property was created solely and independently by the Supplier/Service Provider.

Anti-Corruption Provisions

1. **Compliance with Anti-Corruption Laws.**

a. The Service Provider represents and warrants that it will take no action, directly or indirectly, that would constitute a violation of the United States Foreign Corrupt Practices Act of 1977, as amended from time to time (the "FCPA"), the United Kingdom Bribery Act 2010, as amended from time to time (UKBA), any other applicable anti-corruption laws or regulations, or NVR's Policy against Bribery and Corruption.

b. Specifically, the Service Provider represents and warrants that in carrying out its responsibilities under this Agreement neither it nor any of its officers, directors, employees, representatives, contractors, designees, ultimate beneficial owners or shareholders, nor any other party acting on its behalf, will directly or indirectly make, offer, authorize, promise to make, or receive any Payment:

   i. to obtain or retain any contract, business opportunity or other similar benefit;
      1. to or for the use or benefit of any Government Official;
      2. to any other person where the Service Provider knows or has reason to know or suspect that any part of such Payment will be directly or indirectly given or paid by such other person, or will reimburse such other person, for any Payment previously made or given to

any Government Official when such Payment could not be made directly in accordance with this Section 1; or

3. to any person where such Payment violates any laws, decrees, regulations or policies having the force of law in the country or countries of such person or applicable to such person or the laws of [the United States of America and] England and Wales].

ii. to or from any person, whether or not a Government Official,

1. with the intention to bring about or reward the improper performance of a duty or obligation to which the person is subject; or
2. with the knowledge or belief that the acceptance of the advantage in itself constitutes the improper performance of the person's duty or obligation.

c. Definitions. For the purposes of this Section 1, the following definitions shall apply:

d. The "Government" is any national, federal, state, provincial, municipal, local, or any other Government, including any department, agency, instrumentality, company, corporation, or other entity owned or controlled by any government;

i. A "Government Official" is any

1. official, employee, or representative of any Government or state owned enterprise;
2. political party, or any Official, employee, or representative of any political party;
3. candidate for political office;
4. Official, employee, or representative of any international organization.

ii. An "Affiliated Person" is any officer, director, or employee of, or owner of any beneficial interest in or with respect to, the Service Provider, including any Personnel.

iii. A "Payment" is any monetary payment, loan, donation, gift, in-kind service, or any other thing of value, or any financial or other advantage.

2. **Facilitating Payments**. Service Provider shall not make Facilitating Payments. A Facilitating Payment is a small value payment made to a Government Official to expedite or secure the performance of routine, or non-discretionary Governmental action, which is ordinarily and commonly performed by a Government Official.

3. **No Anti-bribery Offences**. The Service Provider represents and warrants that it has not been convicted of, pleaded guilty to, or charged with any offence involving fraud, corruption or bribery in any jurisdiction or country.

4. **Fully Qualified and Authorized**. The Service Provider represents and warrants that it is fully qualified to assist NVR and is authorized to act in the capacity contemplated by the Agreement in accordance with all applicable laws. Further, the Service Provider has complied with any applicable registration and licensing requirements.

5. **Immediate Disclosure by Service Provider**. The Service Provider agrees to immediately inform NVR if a possible violation by the **Service Provider** of the FCPA, UKBA, other applicable anti-bribery law, and/or NVR's Supplier Code of Conduct including the anti-corruption provisions thereof has taken place. Further, if any Government Official or any relative of such Government Official solicits, asks for, or attempts to extort, any money or thing of value from the Service Provider, the Service Provider shall refuse such solicitation, request or extortionate demand, and immediately report the event to NVR.

6. **NVR's Right to Disclose**. The Service Provider agrees that full disclosure of information relating to a possible violation by the Service Provider of applicable law, including a violation of the FCPA, UKBA, or any other applicable anti-bribery law, may be made by NVR at any time and for any reason to the U.S. or UK Government, its agencies, and/or any other Government or non-Government party.

7. **Compliance Training for the Service Provider's Personnel**. The Service Provider warrants that it fully understands these provisions relating to its business conduct and will ensure that it and all Affiliated Persons fully understand and comply with these provisions in the same manner as they apply to the Service Provider herein. The Service Provider agrees to make itself available, and shall procure to make the Personnel available, for compliance training as directed by NVR as directed by NVR.

8. **Certification of Non-Violation**. If requested by NVR, the Service Provider warrants that its senior personnel, including all Personnel, will furnish NVR a signed non-violation certification on an annual basis.

9. **Records and Audit**. The Service Provider shall keep accurate accounts, books, and records showing all costs and charges incurred in accordance with generally accepted accounting principles and practices. Such accounts and records shall be made available in the Service Provider's office during normal business hours for inspection by NVR or its designee. The Service Provider shall preserve such accounts and records for at least five (5) years after the end of the term of this Agreement. NVR shall further have the right, upon reasonable written notice to the Service Provider, to audit compliance by the Service Provider with all provisions of this Agreement including, but not limited to, provisions of this Agreement related to compliance with the FCPA, UKBA, and any other applicable anti-bribery laws. The Service Provider agrees to fully cooperate with respect to any such audit or other compliance review.

10. **Accuracy of Representations at All Times**. The Service Provider undertakes that all of the listed Representations and Warranties will remain true, accurate, and complete at all relevant times.

11. **Termination**. At its sole discretion, upon notification to the Service Provider, NVR may terminate this Agreement effective immediately if:
    a. NVR makes a good faith determination that the Service Provider, and/or any Affiliated Person, has breached these Representations and Warranties and/or otherwise has committed a violation of the FCPA, UKBA, and/or any other applicable anti-bribery laws; OR
    b. The Service Provider fails or refuses to promptly furnish the anti-bribery non-violation certification referenced in Section 8 above.

PRICING, FEES AND PAYMENT TERMS

Fees

- The total fees for the project is Rs. 3,50,000/- plus 18% GST .

Payment Terms:

- 10% amount to be invoiced as advance on signing of MOU.
- 70% amount to be invoiced as first installment on completion of data collection
- 20% amount to be invoiced on submission of report and receipt of feedback on quality check (by IQVIA).
- In case, the number of students increase or decrease by the time implementation begins or if the number of districts are increased or decreased (as per mutual written consent), the fees will be calculated on a pro-rata basis.
- All invoices raised by the Service Provider shall be accompanied by relevant back up documentation and all other documents supporting the payment.
- The invoice shall identify the Services performed, the dates on which the Services were supplied and the rates applicable.
- The invoice shall also mention all relevant information like Work Order Number, Service Tax Registration Number, VAT Registration Number, GSTIN etc.

- The payment terms for the contract would be 7 days post submission of the invoice on the completion of the milestone, and undertaking that no health establishments (medical colleges, multi-specialty & district hospitals) have been left during the field work of the respective districts and on approval of quality of field work from NVR, the payment would have to be credited in 7 days' time post the submission of invoice.
- Final payment will be credited post quality check and approval from NVR and submission of certificate from all FIs specifying that they have received 90% of dues from the Service Provider

	NVR & Associates Limited		**PSG College of Pharmacy**
By:		By:	DR. M. RAMANATHAN
Title:		Title:	PRINCIPAL
Date:		Date:	06.03.19

- **Witness:**

1. Dr. V. SIVAKUMAR
Associate Professor
PSG College of Pharmacy
Coimbatore.

Gmail

principal cp <principalpsgcp@gmail.com>

MOU - PSG College Of Pharmacy - Coimbatore

1 message

sivavega <sivavega@gmail.com> 8 March 2019 at 15:50
To: "Marimuthu, Ganesh EX2" <ganesh.marimuthu@iqvia.com>
Cc: sanjay@nvrmail.com, rdhiman@in.imshealth.com, hemant.chaudhry@in.imshealth.com, principal cp <principalpsgcp@gmail.com>

Dear Sir,
Please find the attachment of scanned copy of MOU, GST declaration and PAN details.

The account details are as follows
1. Account Holders Name - PSG College of Pharmacy
2. Name of the Bank - Central Bank of India, Peelamedu branch, Coimbatore
3. Bank Account Number - 1481305371
4. IFSC Code - CBIN0280913
5. Email ID - principalpsgcp@gmail.com

T ks & Regards

DR. V. SIVAKUMAR.
ASSOCIATE PROFESSOR
PSG COLLEGE OF PHARMACY
COIMBATORE
9791263777

PSGCP MOU (1).PDF
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Neurochemical Research
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ORIGINAL PAPER

Tribulusterine Containing *Tribulus terrestris* Extract Exhibited Neuroprotection Through Attenuating Stress Kinases Mediated Inflammatory Mechanism: In Vitro and In Vivo Studies

R. Ranjithkumar[1] · Qasim Alhadidi[2] · Zahoor A. Shah[2] · Muthiah Ramanathan[1]

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Abstract

The present study has been aimed to explore the different secondary messengers of the inflammatory pathway NF-κB, kinases (JNK, P38MAPK, GSK3β/βcatenin), apoptosis pathway (Caspase-3 and AIF), and neuronal survival pathway (BDNF) in order to understand the neuroprotective mechanism of aqueous extract of *Tribulus terrestris* (AQTT). In primary cortical neurons, the ischemic condition was induced through oxygen–glucose deprivation (OGD). Anti-inflammatory activity of AQTT was evaluated in formalin induced inflammation model and carrageenan-induced paw edema test. The bilateral common carotid artery occlusion model was employed for whole animal studies. Treatment of AQTT (100 mg/kg) significantly reduced the inflammation induced by formalin and carrageenan. The neuroprotective mechanism of AQTT (50 and 100 mg/kg) was assessed by pre- and post-administration. The results indicate down regulation of kinases and NFkB, suggesting possible anti-inflammatory activity of AQTT. Additionally, AQTT down regulated both caspase dependent and independent apoptotic pathways suggesting its possible anti-apoptotic activity. The treatment of AQTT also reduced GSK3β levels and increased p-Ser9 GSK3β levels; stabilizing the unphosphorylated form of β-catenin and its translocation into the nucleus suggesting role of AQTT in neuronal survival and GSK3β mediated anti-inflammatory property. In comparison to pretreatment, post treatment of AQTT had lesser effects indicating tribulusterine standardized AQTT may have prophylactic effect. This study can be concluded with the thesis that AQTT has neuroprotective effect through alternating neuroinflammation, apoptosis, and promoting neuron survival. Being that it produced better effect with pretreatment, exploring this with thrombolytic drugs will be beneficial. For the first time AQTT has been reported for this indication.

Keywords *Tribulus* · Nerunjil · Apoptosis · Stress kinases · Neuroprotection · Ischemia

Introduction

Tribulus terrestris (*T. terrestris*) Linn, (Family: Zygophyllaceae) commonly known as Nerunjil, is one of the most widely used traditional medicine in India and China [1]. Our previous study has shown that standardized aqueous *T. terristris* extract attenuated hyperalgesia in diabetic neuropathic pain [2] through down regulation of oxidative stress and inflammatory mediators. Active role of *T. terrestris* in ameliorating mitochondrial dysfunction in H9c2 cells during ischemia has been reported [3]. In a recently reported study, the in silico study, inhibition of c-Jun terminal-NH2 kinase (JNK) pathway with alkaloids of *T. terristris* indicated possible anti-inflammatory activity of the herb [4]. In-vitro studies have shown that *N-trans*-ρ-caffeoyl tyramine isolated from *T.terrestris* exerted anti-inflammatory effects by down regulating COX2 and JNK pathway

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11064-019-02768-7) contains supplementary material, which is available to authorized users.

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RESEARCH ARTICLE

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ENTHAM CIENCE

In Silico Molecular Docking, Synthesis of 4-(4-benzoylaminophenoxy) Phenol Derivatives as Androgen Receptor Antagonists

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Abstract: ***Aim and Objective*:** To study the structural difference, optimization, molecular docking and development of new benzoyl amino phenoxy phenol derivatives as anti-prostate cancer agents.

***Materials and Methods*:** Strategies towards the identification of novel benzoyl amino phenoxy phenol (BAPP), molecular docking was performed with the designed Androgen Receptor (AR) blockers. Pharmacophore-based studies revealed that the nitro- or cyano-substituted anilide groups have influenced the activity profiles of non-steroidal AR antagonists, followed by the molecular docking studies with five AR receptors. Molecular docking studies were carried out using Maestro from Schrödinger. Absorption, Distribution, Metabolism, and Excretion (ADME) properties of the BAPP derivatives were evaluated for the predictive bioavailability/drug-likeness. These studies supported vital information for designing new anti-prostate cancer agents.

***Results and Discussion*:** There are 125 compounds were screened and best fit compounds (12 entries) were well-synthesized in good to excellent yields and anticancer activities were evaluated. The compounds, **6i** showed the highest activities of this series (14.65 ± 1.35 μM).

***Conclusion*:** The present approach is simple and efficient for the synthesis of BAPP derivatives and the observed IC_{50} values of BAPPs were in good agreement with the glide scores obtained from the molecular docking. We, further, intend to carry out *in vitro* and *in vivo* AR binding studies for the active compounds.

Keywords: Androgen receptor, prostate cancer, AR antagonist, molecular docking, Benzoyl amino phenoxy phenol, anti-prostate cancer agents.

1. INTRODUCTION

Prostate cancer (PCa) is the second leading causes of cancer deaths in developed countries, and its therapy remains a challenge. National Cancer Institute (NCI) has estimated that 164,690 men will be diagnosed with and 29,430 men will die of prostate cancer in the USA in 2018 [1]. Antiandrogens such as abiraterone acetate, cyproterone acetate, flutamide, nilutamide, and bicalutamide have been clinically accessible for the last 10 years [2, 3]. Unfortunately, these drugs lose their efficacy after a few years of treatment due to resistance and mutation. These drawbacks emphasize the need for new drug development with low adverse effects. The combination of both prostate-specific antigen (PSA) test and a digital rectal examination (DRE) improves the overall rate of PCa detection. Also, the well-established Androgen Receptor (AR) pathway in castrate-resistance tumours is frequently mutant with T877A and W741C/L. Sipuleucel-T is the first therapeutic cancer vaccine to receive FDA approval for the treatment of asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer (CRPC) and used for immunotherapy to boost the body's natural defences to fight against cancer. Several reports suggested that amide analogues have a significant role in different therapeutic applications such as vascular endothelial growth factor receptor 2 (VEGFR-2) inhibitor, *in vitro* antimycobacterial, and antimicrobial activities [4-6]. Also, 6-(3,4-dihydro-1H-isoquinolin-2-yl)-N-(6-methyl pyridin-2-yl)nicotinamide (DIMN) has been proven to be a novel anti-androgenic

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1875-5402/19 $58.00+.00

AMITY UNIVERSITY
KOLKATA

Dated: 23rd March 2018

To
The Principal
PSG College of Pharmacy
Coimbatore

Dear Sir,

This letter is intended as an mutual agreement between the principal investigator (PI, Amity University Kolkata, AUK) and PSG College of Pharmacy as Co investigator (Co-PI) for the submission of joint collaborative project titled "**Designing of smart bandage for wound management"** to BRNS (DAE). For this purpose, the Co-PI is hereby requested to send necessary requirements for the project to the PI. Once the proposal gets funding from BRNS, the materials requested by the Co-PI will be procured through PI (via AUK), and will be subsequently forwarded to the Co-PI through proper channel for successful execution of the project.

Thanks and with Regards

Prof. (Dr.) Rama Ranjan Bhattacharjee

AMITY UNIVERSITY WEST BENGAL

Dy. REGISTRAR
AMITY UNIVERSITY KOLKATA

Course

Collaborative project with Amity

PART VI: DECLARATION/CERTIFICATION

It is certified that

1. The research work proposed in the scheme/project entitled **"Development of Smart Bandage for Surface Wound Management"** does not in any way duplicate the work already done or being carried out elsewhere on the subject.
2. The same project proposal has not been submitted to any other agency for financial support.
3. The emoluments proposed for the manpower are as admissible to persons of corresponding status employed in the institute/university or as per the Ministry of Science & Technology guidelines.
4. Necessary provision for the scheme/project will be made in the Institute/ University/ Organization budget in anticipation of the sanction of the scheme/project.
5. If the project involves the utilization of genetically engineered organisms, we agree to submit an application through our Institutional Bio safety Committee. We also declare that while conducting experiments, the Bio safety Guidelines of the Department of Biotechnology would be followed into.
6. If the project involves field trials/experiments/exchange of specimens, etc. we will ensure that ethical clearances would be taken from concerned ethical Committees/ competent authorities and the same would be conveyed to the Department of Biotechnology before implementing the project.
7. If the Project requires any statutory permission(s) for any authority to carry out the project, the same would be obtained and intimated to DBT before taking up research activities.
8. It is agreed that any research outcome or intellectual property right(s) on the invention(s) arising out of the project shall be taken in accordance with the instructions issued by Department of Biotechnology, Govt. Of India.
9. We agree to accept the terms and conditions of Department of Biotechnology, Govt. Of India.
10. The institute/university agrees that the equipment, other basic facilities and such other administrative facilities as per terms and conditions of the grant will be extended to investigator(s) throughout the duration of the project.

11. The Principal Investigator(s) involved in the project has sufficient service duration to carry out the project. In case his tenure get expire before completion of project necessary provision would be made to allow him to complete the project for its logical conclusion.
12. The Institute assumes to undertake the financial and other management responsibilities of the project.
13. The details & information given in the Project proposal are true & factual.

Dy. REGISTRAR
AMITY UNIVERSITY KOLKATA

Signature of Project Coordinator
(applicable only for multi-institutional projects)
Date : 4/6/19

Signature of Executive Authority of Institute/University with seal
Date : 04/06/19

Amity University Kolkata, West Bengal

Signature of Principal Investigator :
Date : 4/6/19.

Signature of Co-Investigator
Date : 6/6/19

Signature of Co-Investigator
Date : 06/06/2019

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COUNTER

Collobrative project @ PSG IAS
2019

PART VI: DECLARATION/CERTIFICATION

It is certified that

1. The research work proposed in the scheme/project entitled **" Chitosan Nanoparticles Loaded with Doxorubicin-folic acid conjugate for Specific Targeting of Breast Cancer cells. "** does not in any way duplicate the work already done or being carried out elsewhere on the subject.
2. The same project proposal has not been submitted to any other agency for financial support.
3. The emoluments proposed for the manpower are as admissible to persons of corresponding status employed in the institute/university or as per the Ministry of Science & Technology guidelines.
4. Necessary provision for the scheme/project will be made in the Institute/ University/ Organization budget in anticipation of the sanction of the scheme/project.
5. If the project involves the utilization of genetically engineered organisms, we agree to submit an application through our Institutional Bio safety Committee. We also declare that while conducting experiments, the Bio safety Guidelines of the Department of Biotechnology would be followed into.
6. If the project involves field trials/experiments/exchange of specimens, etc. we will ensure that ethical clearances would be taken from concerned ethical Committees/ competent authorities and the same would be conveyed to the Department of Biotechnology before implementing the project.
7. If the Project requires any statutory permission(s) for any authority to carry out the project, the same would be obtained and intimated to DBT before taking up research activities.
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11. The Principal Investigator(s) involved in the project has sufficient service duration to carry out the project. In case his tenure get expire before completion of project necessary provision would be made to allow him to complete the project for its logical conclusion.
12. The Institute assumes to undertake the financial and other management responsibilities of the project. The details & information given in the Project proposal are true & factual.

V. Sankar 27/06/2019.

Signature of Project Coordinator

Authority

(applicable only for multi-institutional projects)

Date : 27/06/2019

Signature of Executive

of Institute/University

with seal

Date : 27/06/2019

PSG COLLEGE OF PHARMACY PEELAMEDU COIMBATORE-641 004

Signature of Principal Investigator : V. Sankar

Date : 27/06/2019.

Signature of Co-Investigator

Date : 27/06/2019

Dr. M. Ramanathan, M.Pharm. Ph.D.
Principal
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Signature of Co-Investigator

Date : 27/06/2019

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Research Article

A REVIEW ON POISONOUS BUT BENEFICIAL PLANT – JAYAPALA (*Croton tiglium*)

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Croton tiglium, traditional medicine, jayapala, purgative, pharmacological properties.

ABSTRACT

Plants and their extract have the potential to cure the infirmity of mankind. From ancient times herbal plants are used for treatment. *Croton tiglium* Linn belongs to the family of Euphorbiaceae is widely distributed throughout the plain of India. Jayapala (*Croton tiglium*) is one among the upa vishas and a well-known plant in Indian system of medicine as certain number of formulations includes this drug as an ingredient after proper purification. The word Upavisha means nearer to visha i.e. drugs which possess the same qualities of visha, but not that much potent. Also it is one of the known purgative drugs in Ayurveda with huge therapeutic values. This review article includes overall information about the plant *Croton tiglium*, its botanical description, toxicological aspect, treatment in both Ayurveda and Modern toxicology, its shodhana (purification) processes, FT- IR, GC-MS for component identification.

INTRODUCTION

Plants are the prime source of medicine in Ayurveda. Several compounds have been isolated from medicinal plants and introduced for the service of mankind; however most of these medicines have been withdrawn due to their toxicity or side-effects. Traditionally, plants having various classes of phytochemicals are still in use either in their crude form or after proper processing. Though most of the plant drugs are safe, yet few are toxic for human health. These poisonous/toxic plants are categorized as *viṣa* (poison) and *upaviṣa* (toxic but not lethal for human health) in Ayurvedic texts (table 1) and also listed in the schedule-E of Drugs and Cosmetics Act 1940 (table 2). Jayapala (*Croton tiglium*) is one among the upavishas and a well-known plant in Indian System of Medicine

Table 1 List of plants having Visa properties

Visa	Binomial nomenclature	Family
Vatsanabha	Aconitum ferox wall	Ranunculaceae
Mustaka	Aconitum chasmanthum stapfex Holmes	Ranunculaceae
Srngivisa		
Kalakuta		
Saktuka		

Table 2 List of plants having Upavisa properties.

Upavisa	Binomial nomenclature	Family
Arka	Calotropis procera	Asclepiadaceae
Snuhi	Euphorbia neriifolia Linn.	Euphorbiaceae
Langali	Gloriosa superb Linn.	Liliaceae
Karavira	Nerium indicum mill.	Apocynaceae
Gunja	Abrus precatorius Linn.	Fabaceae
Ahiphena	Papaver somniferum Linn.	Papaveraceae
Dhattura	Datura metal Linn.	Solanaceae

Table 3 Ayurvedic poisonous plant listed in the schedule E of D&C Act 1940

Poisonous Plants	Binomial nomenclature
Aphipena	Papaver somniferum
Arka	Calotropis procera
Bhallataka	Semecarpus anacardium
Bhanga	Cannabia eativa Linn.
Danti	Baliospermum monatanum Mull.Arg
Dhattura	Datura metal Linn.
Gunja	Abrus precatirius Linn.
Jayapala	Croton tiglium
Karavira	Nerium indicum
Langali	Gloriosa superba
Parasika yavani	Hyoscyamus nibar Linn.
Snuhi	Euphorbia neriifolia Linn.
Vatsanabha	Aconitum chasmanthum
Visamusti	Strychnos nux-vomica

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frontiers in Chemistry

ORIGINAL RESEARCH
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Design, Synthesis, and Biological Evaluation of (E)-N'-((1-Chloro-3,4-Dihydronaphthalen-2-yl)Methylene)Benzohydrazide Derivatives as Anti-prostate Cancer Agents

*H. A. Arjun[1], Ramakrishnan Elancheran[1], N. Manikandan[2], K. Lakshmithendral[1], Muthiah Ramanathan[2], Atanu Bhattacharjee[3], N. K. Lokanath[4] and Senthamaraikannan Kabilan[1]**

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Prostate Cancer (PCa) is the most frequently diagnosed cancer in men in their late '50s. PCa growth is mainly due to the activation of the androgen receptor by androgens. The treatment for PCa may involve surgery, hormonal therapy, and oral chemotherapeutic drugs. A structural based molecular docking approach revealed the findings of *(E)-N'-((1-chloro-3,4-dihydronaphthalen-2-yl)methylene)benzohydrazide* derivatives, where the possible binding modes of the compounds with protein (PDB ID: 3V49) are shown. The compounds (*6a-k*) were synthesized and characterized by using conventional methods. The compounds, *6g, 6j*, and *6k* were reconfirmed through single crystal X-ray diffraction (XRD). Further, the compounds *(6a-k)* and standard drug were evaluated against human prostate cancer cell lines, LNCaP and PC-3 and the non-cancerous cell line, 3T3. Among these compounds, *6g* and *6j* showed higher cytotoxicity, and *6g* exhibited dose-dependent activity and reduced cell viability. The mechanism of action was observed through the induced apoptosis and was further confirmed by western blot and ELISA. Molecular dynamics simulation studies were carried out to calculate the interaction and the stability of the protein-ligand complex in motion. ADME properties were predicted for all the tested compounds. These findings may give vital information for further development.

Keywords: androgen receptor, prostate cancer, benzohydrazide, molecular docking, molecular dynamics, ADME

INTRODUCTION

Cancer is a group of heterogeneous diseases leading to abnormal cell growth and dysfunction which proliferates to other parts of the body. Prostate cancer (PCa) is the second leading cause of cancer deaths among men in the United States. The American Cancer Society has estimated that 174,650 men will be diagnosed and there will be 31,620 deaths due to PCa in the United States in 2019

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11.01.2020

Certificate

With high regards, we are certifying that **Dr.G.Syamala, Associate Professor,** Department of Pharmacognosy, PSG College of Pharmacy, Peelamedu, Coimbatore, has been invited as an external faculty to deliver lecture for II B.Sc. Botany students regarding Job oriented course entitled "phytopharmaceutical science", organized in the **Department of Botany, PSGR Krishnammal College for Women, Coimbatore.** She has delivered lectures on following dates

1st, 23rd and 24th of July 2019

5th and 19th September 2019

8th & 9th of October 2019

Looking forward for further collaborative activities

Signature

JOC Co-ordinator

Dr.M.Kamalam

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11.01.2020

Certificate

With high regards, we are certifying that **Mrs.S.Vanitha, Assistant Professor,** Department of Pharmacognosy, PSG College of Pharmacy, Peelamedu, Coimbatore, has been invited as an external faculty to deliver lecture for II B.Sc. Botany students regarding Job oriented course entitled "Phytopharmaceutical science", organized in the **Department of Botany, PSGR Krishnammal College for Women, Coimbatore.** She has delivered lectures on following dates.

15th, 30th &31st of July 2019

13th, 14th, 20th, 21st and 27th of August 2019

Looking forward for further collaborative activities

Signature

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TOPICAL DELIvERy Of DRUGS USING ETHOSOMES: A REvIEW

Article *in* Indian Drugs · October 2019

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REVIEW ARTICLE

TOPICAL DELIVERY OF DRUGS USING ETHOSOMES: A REVIEW

V. Sankar[a]*, V. Wilson[a], K. Siram[a], A. Karuppaiah[a], S. Hariharan[b], A. Justin[c]

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ABSTRACT

The skin is the largest organ of human body that restricts the movement of drug to the systemic circulation. Topical drug delivery system is a system where the drug reaches the systemic circulation through the protective layer i.e. skin. The main disadvantage of this route is the low diffusion rate of the drugs across the layer of skin which is the stratum corneum. To overcome this problem to a certain extent, ethosomal delivery for drugs and herbal compounds has been recently introduced. Literature studies state ethosomal formulation of acyclovir show high therapeutic efficiency with shorter healing time in the treatment of recurrent herpes labialis than conventional Zovirax. Also, the ethosomes of minoxidil enhanced the skin permeation of minoxidil *in vitro* in comparison to its ethanolic or phospholipid ethanolic micellar solution or hydroethanolic solution. The advantages of this system include increased drug permeation, increased drug entrapment, and improved drug delivery. Ethosomal drug delivery system opens up doors for the development of new and novel therapies for treating male pattern baldness, as it is an easier way to prepare in addition to its safety and efficacy. In this review article we have focused on topics ranging from methods of preparation of ethosomes, characterization techniques, applications, details about the various research trials for the management of androgenic alopecia and various ethosomal products in market.

Keywords: ethosomes, androgenic alopecia, topical route, skin, ethanol.

INTRODUCTION

Topical route of delivery system is a non-invasive method that enables the drug to reach the systemic circulation. In pharmaceutical point of view topical drug delivery offer advantages compared with other routes of administration, including avoidance of first-pass metabolism, fewer administration frequency, smaller fluctuations in plasma drug profile, and good patient compliance[1]. Skin is a multilayered structure composed of stratum corneum, the outermost and the tightest layer of skin and below which lies the epidermis and dermis[2]. Skin is a highly hydrophobic layer composed of differentiated non-nucleated cells and corneocytes, which are filled with keratins and embedded in the lipid domain. Since the rate limiting step for skin absorption of most molecules is considered to be because of this non-viable layer, percutaneous permeation of molecules is believed to be governed by diffusion laws. The skin contributes to 4% of the total body weight. The extent of skin permeation of a compound may depend on the route of absorption. The barrier nature of skin makes it difficult for most drugs to penetrate into and permeate through it[3]. In order to improve topical drug delivery, many kinds of techniques, including complex physical enhancement strategies, such as iontophoresis[4], sonophoresis[5], microneedle[6], and electroporation[7], and lipid vesicular systems such as emulsions[8], microemulsions, and liposomal-based delivery systems, have been used to overcome the barrier of SC. Amongst these, liposomal-based delivery systems, including conventional liposomes[9], ultraflexible liposomes[10], and ethosomes[11-14], offer a promising strategy for improving skin drug delivery and have attracted much interest in recent years due to the merits, including convenience for use and harmlessness to skin. There are three pathways which are involved in the transdermal permeation of drugs: (1) through the intercellular lipid zone in sub cutaneous (SC) region ; (2) through the

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SUMMER RESEARCH FELLOWSHIP PROGRAMME
CERTIFICATE

This is to certify that Mr R Karthick Kannan worked on a project entitled "Splicing analysis of human 45S rRNA" during September - November 2019 as a Summer Research Fellow under the supervision of Dr Indumathi Mariappan, LV Prasad Eye Institute, Hyderabad. The Summer Research Fellowship Programme is jointly sponsored by IASc (Bengaluru), INSA (New Delhi) and NASI (Prayagraj).

M.R.N. Murthy

Place: Bengaluru
Date: 03-01-2020

M.R.N. Murthy
Chairman, Science Education Panel

INDIAN ACADEMY OF SCIENCES
C. V. Raman Avenue, Post Box No. 8005, Raman Research Institute Campus, Sadashivanagar, Bengaluru 560 080, INDIA

SUMMER RESEARCH FELLOWSHIP PROGRAMME
CERTIFICATE

This is to certify that Mr D Arunprasath worked on a project entitled "To look at the endosomal gene expression in Drosophila hematopoietic system" during September - November 2019 as a Summer Research Fellow under the supervision of Professor Maneesha Shreedhar Inamdar, Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru. The Summer Research Fellowship Programme is jointly sponsored by IASc (Bengaluru), INSA (New Delhi) and NASI (Prayagraj).

M.R.N. Murthy
Chairman, Science Education Panel

Place: Bengaluru
Date: 03-01-2020

INDIAN ACADEMY OF SCIENCES
C. V. Raman Avenue, Post Box No. 8005, Raman Research Institute Campus, Sadashivanagar, Bengaluru 560 080, INDIA

SUMMER RESEARCH FELLOWSHIP PROGRAMME
CERTIFICATE

This is to certify that Mr Karthi Keyan worked on a project entitled "Role of ubiquitin proteasome pathway in cancer" during September - November 2019 as a Summer Research Fellow under the supervision of Professor Alo Nag, University of Delhi South Campus, New Delhi. The Summer Research Fellowship Programme is jointly sponsored by IASc (Bengaluru), INSA (New Delhi) and NASI (Prayagraj).

M.R.N. Murthy

Place: Bengaluru
Date: 12-12-2019

M.R.N. Murthy
Chairman, Science Education Panel

INDIAN ACADEMY OF SCIENCES
C. V. Raman Avenue, Post Box No. 8005, Raman Research Institute Campus, Sadashivanagar, Bengaluru 560 080, INDIA

SUMMER RESEARCH FELLOWSHIP PROGRAMME
CERTIFICATE

This is to certify that Ms K Bharathi worked on a project entitled "Optimization of isolation protocols of proteins obtained from human placental tissue for performing proteomics by mass spectrometry" during September - November 2019 as a Summer Research Fellow under the supervision of Professor Shinjini Bhatnagar, Translational Health Science & Technology Institute, Gurgaon. The Summer Research Fellowship Programme is jointly sponsored by IASc (Bengaluru), INSA (New Delhi) and NASI (Prayagraj).

M. R. N. Murthy

Place: Bengaluru
Date: 12-12-2019

M.R.N. Murthy
Chairman, Science Education Panel

SUMMER RESEARCH FELLOWSHIP PROGRAMME
(FINAL YEAR B.PHARMACY)

KARTHICK KANNAN.R	Dr. Indumathi Mariappan, L.V.Prasad Eye Institute, Hyderabad	Splicing Analysis of Human 45s rRNA
K. BHARATHI	Dr.Shinjini Bhatnagar, Translational Health Sciences and Technology Institute, Faridabad.	Optimization of Protein Isolation Techniques from Human Placenta for Proteomics Study by Mass Spectrometry.
ARUNPRASATH.D	Prof. Maneesha Shreedhar Inamdar, Jawaharlal Nehru Centre for Advanced Science and Research, Bengaluru	Endosomal Gene Expression in Drosophila's hematopoietic System
KARTHIKEYAN	Prof. Alo Nag, University of Delhi, South Campus.	Role of Ubiquitin Proteasome Complex in HPV induced Cervical Cancer

G. KUPPUSWAMY NAIDU MEMORIAL HOSPITAL

(Unit of the Kuppuswamy Naidu Charity Trust for Education and Medical Relief)
Accredited by National Accreditation Board for Hospitals & Healthcare Providers (NABH)
Post Box No. 6327, Nethaji Road, Pappanaickenpalayam
Coimbatore - 641 037, INDIA.

Ref:GKNMH/HR/2019 09/10/2019

Dr. M. Ramanathan
Principal
PSG College of Pharmacy
Peelamedu
Coimbatore – 641 004.

Sir,

Sub: Permission for Observership Training- reg.

With reference to your letter dated **03/10/2019**, the Management is pleased to grant permission to your Pharm D Student to undergo training at GKNMH in the department of **Oncology** as per the below mentioned schedule:

NAME	DEPARTMENT	DURATION
Ms. M. T. Gedhanjali	Oncology	14/10/2019 to 13/11/2019

The student are expected to adhere to the following conditions.

1. The Student is requested to contact the Human Resources (HR) for complying with the necessary formalities on the date of reporting for Internship training.
2. The Student have to report and work under the directions of **Dr. A. Rajkumar, Department Chairman & Director of Clinical Operations, HOD of Medical Oncology.**
3. The Student should wear Identification Card (ID) during the training period.
4. The Student should submit Resume, two passport size photos and one ID Proof to the HR.
5. Cell phone usage is strictly prohibited inside the hospital premises.
6. The Student should follow the rules and regulations of the hospital and maintain good discipline during the training period.

Thanking you,

A. NEHRUJI
General Manager - HR

G. KUPPUSWAMY NAIDU MEMORIAL HOSPITAL

(Unit of The Kuppuswamy Naidu Charity Trust for Education and Medical Relief)

Post Box No. 6327, Nethaji Road, Pappanaickenpalayam,
Coimbatore - 641 037. INDIA.

Ref: GKNMH/HR/2019 **13/11/2019**

TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Ms. Gedhanjali. M. T,** Pharm. D student of PSG College of Pharmacy, Coimbatore – 641 004. underwent **Internship Training** in the department of **Oncology** in our Hospital from **14/10/2019 to 13/11/2019.**

We wish her all success for her future endeavors.

A. Nehruji
General Manager - HR

Phone : 0422 - 2245000, 2243501 to 7 Fax : 0422 - 2243509 E-mail : gknmh@vsnl.com Web : www.gknmhospital.org

Prudence mam.

PSG COLLEGE OF PHARMACY

(An ISO 9001 : 2008 Certified Institution)

ACCREDITED WITH 'B' GRADE BY NAAC (1st CYCLE)

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0422-2570170 (6 Lines)
Fax : 0422-2594400
E-mail : principal@psgpharma.ac.in
Website : www.psgpharma.ac.in

03.10.2019

Dr. M. Ramanathan, M. Pharm, Ph.D.,
Principal

To
The Chief Executive Officer,
GKNM Hospitals,
Coimbatore

Dear Sir,

I request you to offer one month internship/training in the Department of Oncology, GKNM Hospitals for our student, Miss M. T. Gedhanjali, Pharm D Intern of PSG College of Pharmacy.

Kindly do the needful.

Thanking you

Yours truly,

Dr. M. Ramanathan
Principal

Dr. M. Ramanathan, M.Pharm, Ph.D.
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4.

Colloids and Surfaces B: Biointerfaces 174 (2019) 443–450

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

Prediction and elucidation of factors affecting solubilisation of imatinib mesylate in lipids

Karthik Siram[a,1], Selvaraj Divakar[b,1], Chellan Vijaya Raghavan[c], Gregory Marslin[d], Habibur Rahman[a,e], Gregory Franklin[d,*]

[a] Department of Pharmaceutics, PSG College of Pharmacy, Peelamedu, Coimbatore, India
[b] Department of Pharmacology, PSG College of Pharmacy, Peelamedu, Coimbatore, 641004, India
[c] RVS Padmavathi Ammal College of Pharmacy, Coimbatore, India
[d] Department of Integrative Plant Biology, Institute of Plant Genetics of the Polish Academy of Sciences, Strzeszyńska 34, 60-479, Poznań, Poland
[e] Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, UCSI University, Kuala Lumpur, 56000, Malaysia

ARTICLE INFO

Keywords:
Imatinib mesylate
Lipids
Solubility
Physico-chemical properties
QSSR model

ABSTRACT

The physico-chemical properties of lipids influencing the solubilisation of imatinib mesylate (IM) in lipid matrix were evaluated and a statistical model to predict the same has been derived in the present study. After experimental quantification of IM solubility in various lipids, Hansen Hildebrand's total solubility parameters were calculated in order to study the role of various forces connected to lipid-drug interaction. To develop a relationship between the various descriptors of the lipids and experimental solubility of IM in lipids (% w/w), quantitative structure-solubility relationship (QSSR) was used. To generate equations that can predict the solubility of IM in lipids (%w/w), multiple linear regression was used. Amongst the various lipids tested, glyceryl monostearate and behenic acid solubilised the highest (6.19 ± 0.22%) and lowest (0.01 ± 0.01%) amounts of IM respectively. Our results suggested that alkyl chain length, polarity of the lipids, index of cohesive interaction in solids, estimated number of hydrogen bonds that would be accepted by the solute from water molecules in an aqueous solution, estimated number of hydrogen bonds that would be donated by the solute to water molecules in an aqueous solution and solvent accessible surface area collectively play a significant role in solubilising IM in the lipids. The equation developed could predict the solubility of IM in lipids with good accuracy (R^2_{pred} = 0.912).

1. Introduction

Lipids are chemically diverse groups of macromolecules classified under several categories namely fatty acids, glycerides, esterified glycerides, hydrogenated oils, waxes, phopsholipids, etc. [1]. They form a major part of our diet and also play a crucial role in the body as building blocks of basic structural elements such as biological membranes, vitamins, hormones, intracellular messengers, enzyme cofactors, emulsifying agents in the digestive tract, electron carriers, etc. Lipids assist in presenting the drugs in a solubilised state to the gastrointestinal tract to achieve enhanced drug absorption. Consequently, the lipids may promote the delivery of drugs to the systemic circulation through the intestinal lymphatics by evading first pass metabolism [2]. Thus, lipids also play an important role in enhancing the bioavailability of drugs that suffer poor aqueous solubility and/ or low intestinal permeability and/ or extensive first pass metabolism [3]. Additionally, the uptake of hydrophilic drugs to brain [4], lymphatics [5], etc., could also be improved by encapsulating them in the lipid matrix.

The number of lipid-based formulations (LBFs) is tremendously increasing over the past few decades due to their biocompatibility, economy, safety, non-toxicity and biodegradability [6]. LBFs generally consist of core lipid(s) and surfactant(s), with or without water, where the solubilisation of drug in the lipid matrix is crucial for the successful design of LBFs [7–10]. Lipids represent a broad term encompassing different categories like fatty acids, partial glycerides (mono, di and triglycerides), mixtures of fatty acids and partial glycerides [11]. Each of these categories additionally has several lipids which vary in their chemical structure and physico-chemical properties. As lipid and drug molecules are chemically diverse, a given lipid need not necessarily solubilise all drugs and vice versa. Although lipophilic drugs can be

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[1] These authors contributed equally to the work.

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Synergistic and enhanced anticancer effect of a facile surface modified non-cytotoxic silver nanoparticle conjugated with gemcitabine in metastatic breast cancer cells

Arjunan Karuppaiah[a,1], Karthik Siram[a,b], Divakar Selvaraj[c,d], Mohankandhasamy Ramasamy[e], Dinesh Babu[f], Veintramuthu Sankar[a,*]

[a] Department of Pharmaceutics, PSG College of Pharmacy, Coimbatore 641 004, Tamil Nadu, India
[b] Institute of Plant Genetics, Polish Academy of Sciences, Strzeszynska 34, 60-479, Poznan, Poland
[c] Department of Pharmacology, PSG College of Pharmacy, Coimbatore, Tamil Nadu, India
[d] Department of Pharmacology, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Ooty, Nilgiris, Tamil Nadu, India
[e] Department of Chemical Engineering, Waterloo Institute of Nanotechnology, University of Waterloo, Waterloo, N2L 5G1, Canada
[f] Faculty of Pharmacy and Pharmaceutical Sciences, Katz Group Centre for Pharmacy and Health Research, University of Alberta, Edmonton, Alberta, T6G 2R3, Canada

ARTICLE INFO

Keywords:
Breast cancer
Gemcitabine
Silver nanoparticles
Synergism
Electrostatic attraction

ABSTRACT

The safety and efficacy of metallic nanoparticles was one of the major challenges that limit their use in the treatment of cancer. Nanotechnology is applied in the field of pharmaceutical sciences with focus on improving the therapeutic outcome in various diseases. Recently, many novel nano-formulations comprising two or more drugs were studied to improve their efficacy with better safety profile. In this study, we investigated the synergistic cytotoxic effect of gemcitabine (GEM) conjugated non-cytotoxic dose of silver nanoparticles (AgNP) in MDA-MB-453 human triple-negative metastatic breast cancer cells. Synthesized AgNP and electrostatic conjugates were characterized by UV-spectroscopy, dynamic light scattering (DLS), Transmission electron microscopy (TEM), Scanning electron microscopy (SEM) and energy dispersive x-ray analysis (EDAX). GEM-(non-cytotoxic AgNP) conjugated system (IC_{50} = 37.64 μM) showed better cytotoxic activity in MDA-MB-453 cells when compared to individual treatments of GEM (IC_{50} = 56.54 μM) or AgNP (IC_{50} = 71.45 μg/ml). The synergism between the GEM-(non-cytotoxic AgNP) for all the tested doses were evaluated using CompuSyn software. The combination index (CI) of ED_{50}, ED_{75} and ED_{90} showed synergism for GEM-(non-cytotoxic AgNP) conjugation. According to the calculated dose reduction index (DRI), it requires 1.70-fold less GEM plus 42.55-fold less AgNP to achieve the same 50 % inhibition at 18.38 (GEM): 1 (AgNP) ratio.

1. Introduction

Nanotechnology is applied in various fields of pharmaceutical sciences to improve the physicochemical and ADME properties, efficacy and safety of the drugs [1]. One such approach is combining effective metallic nanoparticles with chemotherapeutic agents [2]. Metallic nanoparticles possess unique properties due to their size, shape, surface structure and aggregation characteristics [3]. Amongst, AgNP is the one which is extensively studied in pharmaceutical sciences because of its antimicrobial activity and cytotoxicity against various cancer cell lines [4–6]. Nano silver can be easily oxidized in the presence of oxygen leading to the release of silver ions (Ag^+) which is the major source of toxicity. Thus, AgNP often acts as a source of Ag^+ inside the cells. Ag^+ ions induce oxidative stress through the generation of reactive oxygen species and causes damage to cellular components such as cell membrane, protein and DNA. This leads to apoptotic and necrotic cell deaths triggering the release of pro-inflammatory cytokines which cause further damage to nearby tissues or cells. AgNP can also deplete the antioxidant molecules like glutathione and aggravate the cytotoxic effects. AgNP are reported to cause genotoxicity, neurotoxicity, pulmonary toxicity, hepatotoxicity and immunotoxicity [7]. Necropsy analysis of rats orally administered with AgNP (5 mg/kg b.w. and 10 mg/kg b.w.) for 28 days showed no signs of toxicity in the organs such as kidney, brain, lungs, heart and testis. Liver cells had some anomaly in 10 mg/kg b.w. treatment and not in 5 mg/kg b.w. treated rats [8]. Hepatoma cells (HepG2) treated with non-cytotoxic dose (< 0.5 mg/L) of AgNP

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Available online 30 December 2019

Antibiotic Coated Sutures

Request for Research Proposal

Telma Micro Needles

mou

Gmail

principal cp <principalpsgcp@gmail.com>

Meeting request- Telma Micro

1 message

Deepu Iyengar <deepuiyengar@gmail.com> 5 December 2019 at 10:43
To: principal@psgpharma.ac.in
Cc: principal cp <principalpsgcp@gmail.com>

Dear Dr. M Ramanathan,
Request you to kindly let us know a day convenient to you between Monday, 9th and Friday, 13th of December, 2019 for the meeting.

Telma Micro would like to go ahead with this project.
Regards,
Deepu Iyengar
PS: The email request was sent earlier on 28th November, 2019; please see trailing mail.

Dr Sabas
10th Tuesday
Morning 10Am
Pl Morning
to confirm

-------- Forwarded message ---------
. rom: **Deepu Iyengar** <deepuiyengar@gmail.com>
Date: Thu, Nov 28, 2019 at 3:55 PM
Subject: Re: Project proposal - consultancy basis - attached with this mail.
To: principal@psgpharma.ac.in <principal@psgpharma.ac.in>
Cc: Mani <smani1403@gmail.com>

Dear Dr. M Ramanathan,
We have received the proposal, thank you. Telma Micro would like to go ahead with this project.

I request that we have a meeting with our Director Mr. Subramanian S, your team so that we could address any technical nuances of the project before we initiate the same. We will be traveling from Bangalore for this meeting and request you to kindly let us know a day convenient to you between Monday, 9th and Friday, 13th of December, 2019.
Regards,
Deepu Iyengar

On Tue, Nov 26, 2019 at 5:34 PM principal@psgpharma.ac.in <principal@psgpharma.ac.in> wrote:

Sir,
As per your request i have attached the project proposal with antibiotics loaded sutures. Kindly go through this drafts and suggest any correction required. This project will take minimum six month for completion.

From: "Deepu Iyengar" <deepuiyengar@gmail.com>
To: principal@psgpharma.ac.in
Cc: "Mani" <smani1403@gmail.com>
Sent: Monday, September 23, 2019 12:09:21 PM
Subject: Consultancy/ Research support

Dear Dr. M. Ramanathan,

I am writing on behalf of Telma Micro Needles Pvt. Ltd. We would like to engage PSG College of Pharmacy for developing a wound closure product. Under your leadership, PSG College has been successfully developing products in the past, helping many companies deliver products to the market on time.

A brief introduction has been attached to this email, request you to kindly go through the same.

Minutes of the Meeting

For the development of suture TELMA company officials from Bangalore came on 17.12.19 (Tuesday, 10.00 AM) and interacted with Dr. M. Ramanathan, Principal, Dr. V. Sankar, Vice Principal and Dr. C. Jaikanth, Associate Professor about the feasibility and technical expertise for the execution of antibiotic loaded suture project at PSG College of Pharmacy, Coimbatore.

Following points were discussed:

1. Area of interest in suture for gynaecology and general surgery.
2. Formulation and preliminary in vitro evaluation has to be optimized.
3. The necessary support (chemicals, man power) will be provided. Their expertise will also be visiting frequently to monitor the project.
4. First step of the project is to identify suitable antibiotics for coating on the suture based upon clinical usage and infection occurence. To carry out similar projects with *Centella asiatica* along with silver nanoparticles was also discussed.
5. Roller instruments will be provided by company to get reproducible antibiotic loaded suture.
6. Drying and sterilization will be carried out by company followed by testing will be done by PSGCP. Budget for *Centella asiatica* silver nanoparticle project have to be submitted.

The meeting concluded by 11.30 AM

D Vijay V.S 17/12/19.

Research Paper

Preparation and Evaluation of Rosuvastatin Calcium Nanosuspension and Solid Dispersion Tablets by Wet Granulation and Direct Compression Techniques using Tamarind Gum as a Binder

S. ARJUN, S. KARTHIK, K. ARJUNAN, S. HARIHARAN[1], P. SEENIVASAN[2] AND V. SANKAR*

Department of Pharmaceutics, [1]Department of Pharmaceutical Chemistry, PSG College of Pharmacy, Coimbatore-641 004, [2]Department of Pharmacy Practice, Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research, Chennai-600 116, India

The current investigation was attempted to enhance the solubility and dissolution of rosuvastatin calcium through nanosuspension and solid dispersion techniques using tamarind gum as a binder. Rosuvastatin calcium nanosuspension and solid dispersion were prepared using high shear homogenisation and melt fusion techniques, respectively. Various pre-compression tests were performed for the powder blends. Finally, tablets containing these nanosuspensions and solid dispersions were evaluated for various post compression quality control parameters. The nanosuspension had a particle size of 453.3±23.6 nm with a neutral surface charge. Using the lyophilised nanosuspensions and solid dispersion, tablets were prepared by wet granulation and direct compression techniques. The results of *in vitro* drug release studies in pH 6.8 buffer showed enhanced solubility and release of rosuvastatin calcium from the tablets containing nanosuspension and solid dispersion in 60 min, when compared to the control tablets and a marketed tablet. Additionally, the property of tamarind gum to enhance the release of drug was also observed.

Key words: Nanosuspension, solid dispersion, tamarind gum, rosuvastatin calcium

Among the various routes of delivery available, the oral route is the most preferred route of administration, with advantages like high patient compliance and better pharmacokinetic profile[1]. Tablets constitute a major portion of drug delivery systems that are currently available in the market. Factors like economic feasibility, ease of manufacturing, patient compliance and lack of excipient toxicity render tablets as the most preferred form of drug delivery system[2]. Although the science of nanotechnology has achieved new heights for enhancing the bioavailability at the laboratory level, translating the product to tablets for oral administration remains the ultimate goal to cater patients in the clinic.

Solubility is one of the important factors required to achieve desired systematic concentration of a drug in systemic circulation for achieving the desired therapeutic response[3]. Low aqueous solubility is the major problem in formulation development of several new chemical entities[4]. Often, these poorly water soluble drugs need to be administered at high doses to achieve desired therapeutic plasma concentrations after oral administration[5]. A great number of new and possibly beneficial chemical entities do not have suitable pharmaceutical dosage forms because of their poor solubility and poor dissolution rates. The oral absorption of drugs is most often controlled by dissolution in the gastrointestinal tract[6]. Hence, an attempt was made using a model drug with poor solubility and dissolution. Rosuvastatin calcium (RC), a HMG-CoA reductase inhibitor, is widely used in the treatment of hyperlipidemia. RC promotes conversion of HMG-CoA to mevalonic acid by reducing the synthesis of cholesterol. However, RC has poor solubility and bioavailability (20 %)[7,8]. Of late, various kinds of

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CHEMISTRY & BIODIVERSITY

Design, Synthesis, and Biological Evaluation of 2-(2-Bromo-3-nitrophenyl)-5-phenyl-1,3,4-oxadiazole Derivatives as Possible Anti-Breast Cancer Agents

Arjun H. Ananth,[a] Natarajan Manikandan,[b] Ravi Kumar Rajan,[b] Ramakrishnan Elancheran,[a] Kunasekaran Lakshmithendral,[a] Muthiah Ramanathan,[b] Atanu Bhattacharjee,[c] and Senthamaraikannan Kabilan*[a]

[a] Drug Discovery Lab, Department of Chemistry, Annamalai University, Chidambaram 608002, Tamil Nadu, India, e-mail: profdrskabilan@gmail.com

[b] Department of Pharmacology, PSG College of Pharmacy, Coimbatore 641004, Tamil Nadu, India

[c] Computational Biology Laboratory, Department of Biotechnology and Bioinformatics, North-Eastern Hill University, Shillong 793022, India

Breast Cancer (BCa) is the most often diagnosed cancer among women who were in the late 1940's. Breast cancer growth is largely dependent on the expression of estrogen and progesterone receptor. Breast cancer cells may have one, both, or none of these receptors. The treatment for breast cancer may involve surgery, hormonal therapy (Tamoxifen, an aromatase inhibitor, etc.) and oral chemotherapeutic drugs. The molecular docking technique reported the findings on the potential binding modes of the 2-(2-bromo-3-nitrophenyl)-5-phenyl-1,3,4-oxadiazole derivatives with the estrogen receptor (PDB ID: 3ERT). The 1,3,4-oxadiazole derivatives **4a**–**4j** have been synthesized and described by spectroscopic method. 2-(2-Bromo-6-nitrophenyl)-5-(4-bromophenyl)-1,3,4-oxadiazole (**4c**) was reconfirmed by single-crystal XRD. All the compounds have been tested in combination with generic Imatinib pharmaceutical drug against breast cancer cell lines isolated from Caucasian woman MCF-7, MDA-MB-453 and MCF-10A non-cancer cell lines. The compounds with the methoxy (in **4c**) and methyl (in **4j**) substitution were shown to have significant cytotoxicity, with **4c** showing dose-dependent activation and decreased cell viability. The mechanism of action was reported by induced apoptosis and tested by a DNA enzyme inhibitor experiment (ELISA) for Methyl Transferase. Molecular dynamics simulations were made for hit molecule **4c** to study the stability and interaction of the protein–ligand complex. The toxicity properties of ADME were calculated for all the compounds. All these results provide essential information for further clinical trials.

Keywords: 1,3,4-oxadiazole, breast cancer, estrogen receptor, single-crystal XRD, molecular dynamics, ADMET, cytotoxicity.

Introduction

Cancer is a class of diseases that contributes to abnormal cell growth and spread. If the ranges of the abnormal cells are not controlled, it can result in death. The second-largest source of cancer death in women worldwide, after lung cancer, is breast cancer (BCa). The risk of breast cancer deaths in a person is roughly 1 out of 38 in recent years, approximately 2.6%. It is reported from the American Cancer Society that in 2019, around 268,600 people were diagnosed and 41,760 deaths from Breast cancer were recorded.[1] Studies showed that there is a 3.1% rise in the global incidence of breast cancer every year. The ERα (estrogen receptor alpha) is essential for mammary gland development and plays a vital role in breast cancer growth. It was reported that ERα could mediate

Supporting information for this article is available on the WWW under https://doi.org/10.1002/cbdv.201900659

Chemical Data Collections 26 (2020) 100350

Contents lists available at ScienceDirect

Chemical Data Collections

journal homepage: www.elsevier.com/locate/cdc

Data Article

Crystal structure, Hirshfeld surface analysis, DFT and molecular docking studies on benzohydrazide derivatives as potential inhibitors of prostate cancer

H.A. Arjun[a], Ravi Kumar Rajan[b], R. Elancheran[a], M. Ramanathan[b], Atanu Bhattacharjee[c], S. Kabilan[a,*]

[a] Drug Discovery Lab, Department of Chemistry, Annamalai University, Chidambaram, Tamil Nadu 608002, India
[b] Department of Pharmacology, PSG College of Pharmacy, Coimbatore, Tamil Nadu 641004, India
[c] Computational Biology Laboratory, Department of Biotechnology & Bioinformatics, North Eastern Hill University, Shillong 793022, India

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Keywords:
Crystal structure
Hirshfeld surface
Homo-lumo
Molecular docking
Molecular dynamics

ABSTRACT

Single crystals of *(E)-N'-((1–chloro-3,4-dihydronaphthalen-2-yl)methylene)-3-nitro benzohydrazide* and *(E)-3–chloro-N'-((1–chloro-3,4dihydronaphthalen-2-yl)methylene) benzohydrazide* crystals were grown from the (DMSO/ $CDCl_3$) by slow evaporation growth technique. The Compounds 6a ($C_{18}H_{14}ClN_3O_3$) crystallized at orthorhombic system with Pbca space group and 6b ($C_{18}H_{14}Cl_2N_2O$) crystallized at tetragonal system with I 41/a space group through single-crystal X-ray diffraction analysis. The compounds were synthesized and characterized well by spectroscopic techniques. The morphology of crystals were analysed by SEM and the stability at different temperature was done by TG-DTA analysis. Theoretical calculations were performed using density functional theory by Gaussian 09 to develop the optimized geometry, polarizability and dipole moment. Molecular docking and in *vitro* studies were carried out for both the crystals. Molecular Dynamics simulations for the highest binding energy molecule 6a were studied with protein 3V49. Further, the pharmacokinetic properties were predicted for the compounds 6a & 6b. These findings may give vital information for further development.

Specifications table

Subject area	*Organic Chemistry, Crystallography, Hirshfeld surface.*
Compounds	*(E)-N'-((1-chloro-3,4-dihydronaphthalen-2-yl)methylene)−3-nitrobenzohydrazide and (E)−3-chloro-N'-((1-chloro-3,4-dihydronaphthalen-2-yl)methylene)benzohydrazide*
Data category	*Crystal, NMR (^1H & ^{13}C), crystallographic data, computational simulation physicochemical and molecular dynamics.*
Data acquisition format	*Process and analysis data.*
Data type	*Single crystal X-ray diffraction method.*
Procedure	*The compound was synthesized and characterized by spectral Analysis. Both the crystals were confirmed by X- ray diffraction studies. Further molecular docking, ADME properties were checked for these two compounds. Compounds showed activity against (PC3 cell line) Prostate cancer. The bio active molecule was further analyzed in molecular dynamics stimulation.*
Data accessibility	*The Crystallographic data for compound 6a & 6b have been deposited with the Cambridge Crystallographic Data center, CCDC No.* ***1,947,850*** *and* ***1,947,851****. Supplementary data associated NMR spectra and computational studies of compounds 6a and 6b are deputed.*

* Corresponding author. Prof. S. Kabilan, Department of Chemistry, Annamalai University, Chidambaram, Tamil Nadu 608002.
E-mail address: profdrskabilan@gmail.com (S. Kabilan).

https://doi.org/10.1016/j.cdc.2020.100350
2405-8300/

Journal of Research in Pharmacy

Research Article

www.jrespharm.com

Development and evaluation of a pH triggered *in situ* ocular gel of brimonidine tartrate

Saravana BHARATH [1], Arjunan KARUPPAIAH [1], Karthik SIRAM [2], Sivaram HARIHARAN [3], Ramesh SANTHANAM [4], Sankar VEINTRAMUTHU [1]*

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ABSTRACT: The aim of the present research work was to prepare and evaluate *in situ* gel forming ophthalmic drug delivery system loaded with brimonidine tartarate (BT). In this work, carbopol and hydroxy propyl methyl cellulose (HPMC), ophthalmic gel-forming mucoadhesive polymers, which gets converted to gel in the lachrymal fluid were used as in the preparation of pH t riggered *in situ* gel formulation. The formulations were then autoclaved at 121°C for 15 min and evaluated for pH, clarity, gelling capacity, drug content, viscosity, and *in vitro* release. The developed formulations exhibited extended release of drug over a period of 8 hours in *in vitro* studies and therefore it could increase the residence time in eye. The optimized formulations were finally tested for its ability to cause irritation in male albino rabbits. The results indicated that the formulations did not irritate or damage the cornea, iris and conjunctiva.

KEYWORDS: Brimonidine tartarate; *in situ* gel; ophthalmic drug delivery; viscosity enhancement; *in vitro* release.

1. INTRODUCTION

Glaucoma is the second most common cause of blindness worldwide, after cataract and there were 60.5 million people with open angle glaucoma and angle closure glaucoma in 2010, increasing to 79.6 million by 2020. Glaucoma is generally treated using traditional surgery, pills, eye drops, laser surgery, or a combination of any of these methods. One of the major challenges in ophthalmic drug delivery systems is to design new soluble ocular carriers without causing blurred vision and to get the drug into the target site to enhance the therapeutic effects [1]. More than 90% of the marketed ophthalmic formulations are available as eye drops. But, majority of the topically applied formulations do not remain in the eye for long time as they washed off from the eye by constant blinking of the eye, high tear turnover the impermeability of the drugs across corneal epithelial membrane, lachrymal drainage, and tear fluid dilution, which usually results in poor ocular bioavailability of the drugs [2]. As a result of these factors, the ocular bioavailability for the drugs administered is very poor.

Brimonidine tartrate (BT) is a selective alpha-2 adrenergic agonist, used to lower ocular pressure by decreasing production of aqueous humor and simultaneously by increasing uveoscleral outflow. Additionally it functions well in treating glaucoma in cardiopulmonary patients. But, patients taking BT continuously suffer from problems like ocular allergy and sub-clinical inflammation in conjunctiva [3]. As marketed form of BT exists only as solution, research works are necessary for the development of delivery systems that can prolong the release of BT for a long time in the eye to reduce the frequency of administration of BT.

Ophthalmic ointments offer high ocular bioavailability of the drugs by increasing the contact time at the cornea, resisting nasolacrimal drainage, and minimizing the dilution by tears. A major disadvantage of the ointment which restricts its usage is blurred vision. Application of ointments in ophthalmic delivery system relies on the fact that the drug particles may be present in the conjunctival sac for a longer time by

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பாரதியார் பல்கலைக்கழகம்
BHARATHIAR UNIVERSITY
COIMBATORE - 641 046, TAMILNADU, INDIA.
State University | Re-accredited with "A" Grade by NAAC | Ranked 14th among Indian Universities by MHRD-NIRF

Endorsement from the Head of the Institution of PI

(To be given on University/ Institute/Organization/College Letter head)

This is to certify that:

1. Institute welcomes participation of **Dr.Geetha Natesan, Professor, Dept. of Botany, Bharathiar University, Coimbatore-641 046, Tamilnadu, India** as the **Principal Investigator** and **Dr. V.Sankar, Professor and Head, Department of Pharmaceutics, Vice Principal, PSG College of Pharmacy, Peelamedu, Coimbatore-641 004, Tamilnadu, India** as the **Co- Investigator**~~/s~~ for the project titled **"Development and evaluation of nanosilver encapsulated gel with phytocompounds enriched fractions of *Vitex negundo* and *Tridox procumbens* for diabetic foot ulcer: An innovative approach"** and that in the unforeseen event of discontinuance by the Principal Investigator, the Co-Investigator will assume the responsibility of the fruitful completion of the project with the approval of SERB.

2. The PI, **Dr.N.Geetha** is a permanent or regular employee of this Institute/University/Organization and has **7** years of regular service left before superannuation.

3. The project starts from the date on which the University/~~Institute/ Organization/College~~ receives the grant from SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi.

4. The investigator will be governed by the rules and regulations of University/ ~~Institute/Organization/College~~ and will be under administrative control of the University/ Institute/Organization/College for the duration of the project.

5. The grant-in-aid by the SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi will be used to meet the expenditure on the project and for the period for which the project has been sanctioned as mentioned in the sanction order.

6. No administrative or other liability will be attached to SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi at the end of the project.

7. The University/~~Institute/Organization/College~~ will provide basic infrastructure and other required facilities to the investigator for undertaking the research project.

8. The University/ ~~Institute/Organization/College~~ will take into its books all assets created in the above project and its disposal would be at the discretion of SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi.

9. The University/ ~~Institute/Organization/College~~ assumes to undertake the financial and other management responsibilities of the project.

Seal of

University/ ~~Institute/Organization/College~~
~~Head of organization~~ / ~~Principal of College~~
Date: 9.3.2020

Signature

9.3.2020

Registrar of University/~~Head of the Institute~~/

Registrar
Bharathiar University
Coimbatore-641 046

Website: www.b-u.ac.in | Email: regr@buc.edu.in | Phone: 0422-2428108 / 2428108 | Fax:+ 91 422 2425706

PSG COLLEGE OF PHARMACY

(An ISO 9001 : 2015 Certified Institution)
Accredited with 'B' Grade by NAAC (1st Cycle)
Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, Chennai
Approved by Pharmacy Council of India and All India Council for Technical Education, New Delhi
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E-mail principal@psgpharma.ac.in

Endorsement from the Head of the Institution of Co-PI

(To be given on University/Institute/Organization/College Letter head)

1.This is to certify that: Institute welcomes participation of **Dr. V.Sankar, Professor and Head, Department of Pharmaceutics, Vice Principal, PSG College of Pharmacy, Peelamedu, Coimbatore-641 004, Tamilnadu, India** as the **Co- Investigator/s**–for the project titled **"Development and evaluation of nanosilver encapsulated gel with phytocompounds enriched fractions of *Vitexnegundo* and *Tridoxprocumbens* for diabetic foot ulcer: An innovative approach"** and that in the unforeseen event of discontinuance by the Principal Investigator, the Co-Investigator will assume the responsibility of the fruitful completion of the project with the approval of SERB.

2.The Co-PI,.**Dr.V.Sankar** is a permanent or regular employee of this Institute and has **13** years of regular service left before superannuation.

3.The Co-PI will be governed by the rules and regulations of College and will be under administrative control of the College for the duration of the project.

4.The grant-in-aid by the SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi will be used to meet the expenditure on the project and for the period for which the project has been sanctioned as mentioned in the sanction order.

5.No administrative or other liability will be attached to SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi at the end of the project.

6.TheCollege will provide basic infrastructure and other required facilities to the investigator for undertaking the research project.

7.The University will take into its books all assets created in the above project and its disposal would be at the discretion of SCIENCE & ENGINEERING RESEARCH BOARD (SERB), New Delhi.

8. College assumes to undertake the financial and other management responsibilities of the project.

Seal of Signature

Head of the Institute / Principal of College

Dr. K. Rajamanickam, M.Pharm, Ph.D.
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4.

Date: 27/2/2020

PSG COLLEGE OF PHARMACY
PEELAMEDU
COIMBATORE - 641 004

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RESEARCH ARTICLE

Experimental antivenoms from chickens and rabbits and their comparison with commercially available equine antivenom against the venoms of *Daboia russelii* and *Echis carinatus* snakes

Ankit Choraria[a], Rajeswari Somasundaram[a], Mrinmoy Gautam[b], Muthiah Ramanathan[b], Bilal Ahmad Paray[c], Mohammad K. Al-Sadoon[c] and A. Michael[a]

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ABSTRACT

In the present work, chicken (IgY) and rabbit (IgG) antibodies were generated against the venoms of *Daboia russelii and Echis carinatus* snakes and efficacy was compared with commercial antivenom. Antivenom antibodies were purified and evaluated by ELISA, SDS-PAGE, Western Blot. All antivenoms neutralized a challenge dose of $3LD_{50}$. Each ml of IgY, IgG and commercial antivenom neutralized 0.3, 0.34, and 0.6 mg of *E. carinatus* venom and 0.2, 0.22 and 0.57 mg *D. russelii* venom respectively. The present study suggests the generated antivenoms as effective in neutralizing the venoms injected, implying the scope of IgY antivenoms for further screening and evaluation.

ARTICLE HISTORY
Received 8 March 2020
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KEYWORDS
IgY; IgG; commercial antivenom; ELISA; western blot; neutralization

1. Introduction

Envenomation from snakebite is considered a serious health hazard in tropical and sub-tropical regions such as Africa, Asia, Latin America and Oceania affecting around 1.8–2.7 million people worldwide resulting in 81,000 to 138,000 deaths annually (Gutierrez 2017). Currently, available treatment for the envenomation caused by snake venom is the administration of antivenom produced from hyperimmune plasma of equines, which leads to undesirable side effects such as anaphylactic reactions and serum sickness (Laustsen *et al*. 2018), and if the antivenoms are well designed, they can be an effective life-saving drug. The most affected of all the regions in India, which is also the snake bite capital of the world with mortality ranging from 35,000 to 50,000 deaths annually (Choudhury *et al*. 2017). The principal common snakes responsible for causing snake envenomation in India are Indian cobra (*Naja naja*), Common Krait (*Bunagarus caeruleus*), Russell's viper (*Daboia russelii*) and Saw scaled viper (*Echis carinatus*). Snake venom is a mixture of various proteins, organic and inorganic materials. The closely related species of snakes share common proteins that vary within individual snakes depending on different environments and seasons (Pawade *et al*. 2016). The poor neutralizing ability and adverse reactions of equine antivenom have resulted in search of alternative methods for the production of antivenom. A number of research groups have produced antivenom from different animal or avian sources such as Camelid (Padula and Winkel 2016, 2017), Rabbits (Beghini *et al*. 2008, Venkatesan *et al*. 2014), Mice (Tanaka *et al*. 2016, Melo *et al*. 2017), Donkeys (Patrick Fernandez *et al*. 2009), Sheep (León *et al*. 2000), Ducks (Y-Neng Chiou 2008) and chickens (Maya *et al*. 2002, Almeida *et al*. 2008, Meenatchisundaram *et al*. 2008, Araujo *et al*. 2010, Prabhu *et al*. 2010, Duan *et al*. 2016, Navarro *et al*. 2016) so as to produce antivenom of high neutralization potential.

Identification of snakes, post snake bite envenomation depends on the information given by the patients and the conventional method of identification of venoms such as the 20 min whole blood clot test (WBCT) (Pawade *et al*. 2016, Shaikh *et al*. 2017). So far, since antivenoms have been in use for the treatment of snake envenomation, researchers are still exploring the possibilities to develop a rapid snake venom detection kit. Globally, only Australia has a Snake venom detection kit (SVDK) developed by Bio Commonwealth serum laboratories (BIO-CSL). Indian scenario on detection kits for snake venom remains silent though there a couple of antivenom

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ORIGINAL PAPER

Development and Characterization of Phytoniosome Nano Vesicle Loaded with Aqueous Leaf Extracts of *Justicia adhatoda* and *Psidium guajoava* Against Dengue Virus (DEN-2)

Dhanya K. Wilson[1] · Govindarajan Shyamala[2] · Manickam Paulpandi[3] · Arul Narayanasamy[3] · Karthik Siram[1] · Arjunan Karuppaiah[1] · Veintramuthu Sankar[1]

Received: 3 October 2019

Abstract
The leaves of *Psidium guajava* (PG) and *Justicia adhatoda* (JA) are traditionally used in the Indian herbal medicine for the treatment of dengue. The current research work was aimed to evaluate the antiviral activity of the phytoniosomes (PN) loaded with the aqueous extracts of PG and JA (AGN) against dengue virus-2 strain (DEN-2). The AGN were prepared by ultrasonication method using tween 80, poloxamer 407, polyethylene glycol 6000 and cholesterol. The particle size of the PN was found out to be in the range of 105.1 ± 3.6–279.4 ± 5.2 nm. In comparison to the non-PEGylated niosomes, PEGylated niosomes showed lower particle size. AGN showed in vitro antiviral activity against vero cells infected with DEN-2 virus. Capsules containing AGN powder were found to be stable for 3 months when stored at room temperature. AGN4 showed maximum of 40% plaque forming units, indicating that formulation poses significant viral inhibition in in vitro condition.

Keywords Phytoniosomes · Nanoparticles · DEN-2 virus · *Justicia adhatoda* · *Psidium guajava*

Introduction

Dengue is the most frequently observed infection effecting more than 50–100 million cases annually throughout the world [1]. The overall incidences as well as the explosive outbreaks have been increasing dramatically over the last several years. Reported data suggests an estimate of about 500,000 cases of dengue hemorrhagic fever occur world-wide, with 22,000 deaths (Malavige GN, Stephenson JR) [2, 3]. According to data released by the Directorate of the National Vector Borne Disease Control Programme (NVBDCP), India has more than 67,000 cases of dengue fever as of October 13th [4]. Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are caused by a flavivirus named dengue virus (DENV) in which female mosquitoes of the species *Aedes aegypti* and *Aedes Albopictus* act as vector. There are 4 distinct, but closely related serotypes of the virus that cause dengue (DEN-1, DEN-2, DEN-3, and DEN-4). During the course of infection, the patient may experience early symptoms such as fever, headache, rashes, nausea, and musculoskeletal pains, and can even lead to mortality. Recovery of the patients from the infection provides lifelong immunity against that particular serotype. Subsequent infections by other serotypes increase the risk of developing severe dengue [5]. Hematological abnormalities related to platelets like thrombocytopenia, coagulopathy, vasculopathy, and endothelial dysfunction are generally observed in severe dengue [6]. The magnitude of the global problem is compounded by the fact that there is no specific antiviral treatment or vaccines for the disease. The virus attacks and creates lesions in the bone marrow, which causes depletion of the platelets and can even be potentially fatal. It is

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Published online: 02 April 2020

Non-Disclosure Agreement

This Agreement is entered into this on **10th August 2020**, by and between **PSG College of Pharmacy**, a unit under PSG & Sons' Charities, an educational trust with its principal place of business at Avinashi Road, Peelamedu, Coimbatore – 641004 and its Affiliates The Tamil Nadu Dr. M.G.R. Medical University, Chennai which term shall mean and include its successors in interest and assigns of one part

and

M/s Apex Laboratories Private Limited (CIN NO: U85195TN1978PTC007554) having its registered and corporate office at III Floor, SIDCO Garment Complex, Guindy, Chennai-600032,Tamilnadu,INDIA (hereinafter called "Client"/ "apex") which term shall mean and include its successors in interest and assigns of another part

UniversityandApex may hereinafter be referred to as a "Party" or the "Parties."

WHEREAS, the Partieswish to assess a potential business relationship for "Evaluation of apex products" (the "Purpose");

WHEREAS,in connection with the Purpose, Apex will be the disclosing Parties and University will be the receiving parties.

NOW, THEREFORE, in consideration of each Party's undertakings hereunder, and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, and intending to be legally bound hereby, the Parties agree as follows:

1. **Definitions**. For the purpose of this Agreement, "Confidential Information" shall mean any business or technical information, tangible or intangible (including, without limitation, trade secrets; inventions and ideas; technical data and specifications; know-how; formulae; processes; designs, methods; samples, specimens, or physical materials; testing methods; business or financial information; research and development results; product and marketing plans; and customer and supplier information) that is furnished by one Party or any of its Affiliates (defined below) to the other Party, regardless of whether such information is in written, oral, electronic, physical, or other form. All such Confidential Information will be marked "Confidential" at the time of disclosure if disclosed in writing or, if not disclosed in writing, it will be identified by Disclosing Party (as hereinafter defined) as confidential at the time of disclosure, then

reduced to writing, marked "Confidential" and sent to Receiving Party (as hereinafter defined) within thirty(30) days of the original disclosure. This Agreement shall include Confidential Information acquired by a Party during any and all tours of the other Party's facilities. Not by way of limitation of the foregoing, it is acknowledged and agreed that samples, models, both digital and physical, and prototypes of products, and any parts thereof, together with any process diagrams related thereto, embody, and are included within the definition of, the Confidential Information and, further, may constitute the trade secrets under applicable law. "Affiliate," with respect to a Party, shall mean any company which, directly or indirectly, controls or is controlled by or is under common control with such Party by means of ownership of more than fifty percent (50%) of the voting stock or similar interest in said Party.

2. **Disclosure**. Each Party disclosing information (a "Disclosing Party") will make Confidential Information available to the other Party (a "Receiving Party") to the extent that Disclosing Party, at its sole discretion, reasonably considers appropriate for the Purpose.

3. **Obligation of Confidentiality and Non-Use**. Receiving Party agrees to use the Confidential Information only for the Purpose and for such other purpose which Disclosing Party authorizes in writing and not for any other purpose whatsoever. Receiving Party shall not use the Confidential Information in any manner which is detrimental to Disclosing Party. Receiving Party shall not reverse engineer, de-compile, disassemble, or otherwise attempt to analyze the structure, function, or operation of the Confidential Information. Receiving Party also agrees that it shall limit dissemination of the Confidential Information only to those of its employees, agents, consultants, and affiliates ("Representatives") who have a need to know in relation to the Purpose.

   Receiving Party shall inform all such Representatives of the confidential nature of the Confidential Information. Receiving Party further agrees that it shall use the same degree of care to protect the Confidential Information as Receiving Party uses to protect its own proprietary information, which in any event shall be no less than a reasonable degree of care, and to prevent communication of any Confidential Information, or any portion thereof, to any third party. Receiving Party shall take adequate steps to ensure that any such Affiliate, Representative, or related entity to which Receiving Party discloses any Confidential Information is bound to protect such Confidential Information in accordance with the terms of this Agreement prior to any such disclosure and Receiving Party shall be responsible for such disclosure. Receiving Party shall maintain the Confidential Information of Disclosing Party and otherwise comply with the provisions of this Section 3 for a period of seven (7) years from the date of expiration or

termination of this Agreement. In the event of any unauthorized access or disclosure of the Confidential Information, Receiving Party shall provide the Disclosing Party with immediate notice thereof, providing in reasonable detail the circumstances and persons involved.

4. **Permitted Exceptions**. The obligations of Receiving Party, contained in Section 3 above, shall not apply to any Confidential Information which:
   (a) Receiving Party can show was already lawfully known to Receiving Party prior to its receipt of the Confidential Information; or
   (b) Receiving Party can show was independently developed by Receiving Party without use of, or reliance upon, any of the Confidential Information; or
   (c) is publicly available or becomes publicly available without a breach of this Agreement by Receiving Party; or
   (d) is rightfully received by Receiving Party from a third party who is not under a duty of confidentiality to Disclosing Party; or
   (e) is disclosed by Receiving Party with Disclosing Party's prior written approval; or
   (f) is disclosed pursuant to any judicial or governmental requirement or order; provided that Receiving Party takes all reasonable steps to give Disclosing Party sufficient prior notice in order to seek a protective order or contest such requirement or order.

5. **Termination**. This Agreement shall commence as of the Effective Date and shall remain in effect for a period of Ten (10) years from the Effective Date, unless earlier terminated by either Party upon thirty (30) days prior written notice to the other Party hereto. Receiving Party's obligations under this Agreement, with respect to any Confidential Information received by Receiving Party during the term of this Agreement, shall survive any termination hereof for seven (7) years.

6. **Return of Information**. Within ten (10) days of termination of this Agreement, and at the direction of Disclosing Party, Receiving Party agrees to either return to Disclosing Party or destroy (and certify such destruction in writing) all Confidential Information, and all copies thereof as well as all notes, documents, summaries and other recordings of the Confidential Information then in its possession. Receiving Party may retain one (1) archival copy of the Confidential Information that it may use only in case of a dispute concerning this Agreement, subject to Sections 3 and 4 above.

7. **No Grant of License**. This Agreement imposes no obligation on either Party to disclose any of its Confidential Information to the other Party hereto, or to make any use of Confidential Information which it receives from the other Party. No

rights or obligations other than those expressly recited herein are to be implied from this Agreement. Nothing in this Agreement shall be construed to convey to Receiving Party any right, title or interest in any Confidential Information or any license to use, sell, distribute, exploit, copy or further develop the Confidential Information in any way. Furthermore, no license is hereby granted or implied to Receiving Party under any patent, copyright or trademark, any application for any of the foregoing, or any trade name, trade secret or other intellectual property right in which Disclosing Party has any right, title or interest. Nothing herein shall in any way affect the present or prospective rights of the Parties hereto under the patent, copyright or other intellectual property laws of any country.

8. Receiving Party agrees that any breach of Receiving Party's obligations under this Agreement with respect to the Confidential Information may cause serious and irreparable damage to Disclosing Party, the exact amount of which would be difficult to ascertain. Consequently, Receiving Party agrees that in the event of such a breach or threatened breach, Disclosing Party shall be entitled as a matter of right to seek immediate injunctive relief or specific performance, and that these remedies shall be in addition to, and not in lieu of, any other remedies which may be available to Disclosing Party in law or in equity.

9. THE DISCLOSING PARTY MAKES NO REPRESENTATIONS, WARRANTIES OR GUARANTEES REGARDING THE ACCURACY OR COMPLETENESS OF THE CONFIDENTIAL INFORMATION. The Disclosing Party accepts no responsibility for any expenses, losses or actions incurred or undertaken by the Receiving Party as a result of the Receiving Party's receipt or use of the Confidential Information.

6. apex's rights regarding access to and use of such said purpose shall not conflict in any way with this Agreement, of any relevant documents disclosed by university for the purpose of this agreement as applicable federal, state, or local laws etc.,

7. University agrees that any documents or any other relevant papers,information prepared for or on behalf of Apex for this purpose of this agreement will not be used for University'sbusiness purpose or any other purpose without prior written consent of apex .

8. This Agreement does not create a joint venture, partnership, or employee employer relationship between the Parties, nor an obligation to buy or sell products or services, or enter into any other business relationship unless agreed by both parties in writing as separate agreement.

8. **No Waiver**. The failure of Disclosing Party to enforce any of its rights under this Agreement or to take action against Receiving Party in the event of any breach by Receiving Party hereunder shall not be deemed a waiver by Disclosing Party as to any subsequent enforcement of rights or subsequent actions in the event of a future breach.

9. **No Agency; Binding Effect**. This Agreement does not create any agency, partnership or joint venture relationship between the Parties hereto. This Agreement shall be binding upon and enforceable by the Parties hereto, including their respective successors and assigns. Neither Party shall assign or otherwise transfer this Agreement or any of its rights or obligations hereunder without the prior written consent of the other Party hereto.

10. **Governing Law; Exclusive Jurisdiction**. This Agreement shall be construed and governed in accordance with the laws of India, excluding its conflicts of law provisions.

If Any dispute arising out of or in connection with this Agreement shall be exclusively settled by an arbitration administered by the Madras High Court under the IPC Rules of Arbitration by an arbitration tribunal consisting of Sole arbitrator upon mutual consent of both parties (if fail to agree by both parties, then either party can approach the court to appoint sole arbitrator as per IPC Rules on Arbitration. Such arbitration proceedings shall take place in Chennai and be conducted in the English language. Any award of the arbitral tribunal shall be final and binding upon the parties to the arbitration, may be enforced in any court of competent jurisdiction, and judgment thereon may be entered in any court of competent jurisdiction.

11. **Severability**. In the event any terms or provisions of this Agreement shall for any reason be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other terms or provisions hereof.

12. **Entire Agreement; Amendments**. This Agreement constitutes the entire agreement between the Parties hereto and supersedes all prior agreements and understandings, either oral or written, with respect to the subject matter hereof. Any additions or modifications to this Agreement shall not be effective unless made in writing and signed by authorized representatives of the Parties.

13. **Force majeure:** Any party to natural disasters and other force majeure causes of delay in performance of duty, incomplete or non-performance should not be treated as breach of contract.

14. **Counterparts**. For the convenience of the parties, this Agreement may be executed electronically by email or PDF /facsimile transmission/digital of signature pages, and in any number of counterparts, each of which shall be deemed to be an original and which, taken together, constitute one and the same agreement binding on both parties.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives.

For PSG College of Pharmacy

12/8/2020

Name: Dr. M. Ramanathan
Title: Principal

Dr. M. Ramanathan, M.Pharm, Ph.D.
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4.

Witness:

V. SANKAR

Dr. V. Sankar
Vice Principal
PSG College of Pharmacy

P.S.G. COLLEGE OF PHARMACY
PEELAMEDU
COIMBATORE - 641 004.

For Apex laboratories private limited

14/08/2020

Name: Mr. S V Vishagan
Title: Director

For apex laboratories private limited

Witness:

EVP R&D and Business Development

apex laboratories private limited
Chennai-32

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COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH

EXTRAMURAL RESEARCH DIVISION

CSIR COMPLEX, PUSA, NEW DELHI - 110 012

No. 60(0117)/19/EMR-II

Dated : 17-07-2019

From : Head, Human Resources Development Group

To

DR V SANKAR
DEPT OF PHARMACEUTICS
PSG COLLEGE OF PHARMACY
COIMBATORE 641004 T N

Subject : Grants-in-aid for your scheme entitled :MUPIROCIN SILVER NANOPARTICLES LOADED COLLAGEN DRESSING FOR TREATING BURN WOUND INFECTIONS

Sir,

I am directed to refer to your proposal for sanction of CSIR Scheme titled above and to convey the approval of DG CSIR as per the details given below.

I	Duration of the Scheme (from the date of Commencement)	36 Months		
II	Staff	1-SRF / JRF		
III	Contingency (per annum in ₹)	1st Year : 4,00,000	2nd Year : 4,00,000	3rd Year :2,00,000
IV	Equipment (lumpsum in ₹)	~~0~~ NIL		

2. The above sanction is subject to review of periodical progress of the project by expert committee.

3. DG CSIR has also approved the release of the following grants for the period 01/06/2019 to 31/03/2020

No	Grants	Amount (in ₹)
I	Staff	1,40,000
II	Contingency	3,33,333
III	Equipment	~~0~~ NIL
	Total :	**4,73,333**

4. Sanction of grants is subject to strict compliance of the terms and conditions enclosed or as may be modified from time to time. Please go through the instructions carefully with regard to subsequent release of grants and your obligations under this sanction. **The grant for the Ist installment will be sent through EFT (Electronic Funds Transfer), to the concerned authority of your institution on receipt of undertaking (form-A), non-funding certificate and EFT Transaction Request Form.**

The expenditure is debitable to budget head P81102.

Yours faithfully,

SECTION OFFICER (EMR-II)

Encl : As above

Copy to :-

1. Registrar/Principal/~~Director~~ PSG College of Pharmacy, Coimbatore - 641004 (TN) The utilisation of grant is subject to compliance of para- of the terms and conditions stated overleaf.
2. Sr F&AO(EMR) alongwith FVC for first year's grant.
3. Director, CSIR - Institute of Genomics and Integrative Biology, North Campus, Mall Road, Delhi - 110007.

SUMMARY TERMS AND CONDITIONS

1. The first installment of the grants sent by NEFT/RGIS herewith will be utilized subject to submission of the following documents/information.

   a) Acceptance of the grants sanctioned above.

   b) An Undertaking in the prescribed form-A of the enclosed booklet executed on non judicial stamp paper of RS. 10/- each pate duly signed.

   c) A certificate by you duty countersigned by the Head of the Department/Head of the Institution that no other aid giving agency is funding your above scheme.

   d) Date of commencement of the scheme. This should be started within 3 months from the date mentioned in the sanction letter overleaf at Para 3, with or without the appointment of "Staff"

   e) Details of bank account in attached NEFT / RGIS form for transfer of grant.

2. "Contingency" amount will be utilized on pro-rata from the date of the commencement of the scheme. "Staff Stipend" will be utilized from the date the Research Fellow/Associate Joins duty in accordance with the rules stipulated in the terms and conditions and he/she will be paid stipend after receipt of approval of appointment from CSIR. JRF with NET/GATE qualification can be appointed directly, and CSIR concurrence/ratification is to be obtained subsequently.

3. While claiming grants for the subsequent year/period the position regarding unspent balances of the previous year's grants must be mentioned head-wise in the bill failing which the same may be returned UN passed for compliance. Statement of accounts duly audited by the Account Officer and countersigned by the next higher authority in respect of the grants received and expenditure incurred with balance, if any, during the previous year should also be invariably enclosed with the bill.

4. Utilization of funds and maintenance of account under the head "Staff", "Contingency" & Equipment" and appointment of Research Fellows/Associates should be in accordance with the procedure laid down in the terms and conditions.

5. Your obligations under this sanction include, inter alias, the following:

   i. Submission of ***Annual Progress Report*** *(10 Copies) to CSIR* by I st October, each year including the progress of work as on 31st aug. (as per **Form-E1** in the booklet). Non-receipt of this report in time will lead to the scheme being withdrawn.

   ii. Submission of ***Final Technical Reports*** *(4copies)* in **Form-F** of the booklet within 3 months after completion of the work describing the original objectives of the scheme, how far these objectives have been achieved and how the results would benefit technological development or enrich the existing knowledge on the subject.

   iii. Sending of copies of Research Papers published in Journals and Proceedings of Prestigious national/international conferences under this grant with due acknowledgement of CSIR support for information as and when published. The project numbers should always be mentioned in the acknowledgements.

   iv. Submission of the **Audit Utilization Certificate and audited statement of accounts** for the grants paid by the CSIR immediately on termination of the scheme.

6. **ALL INSTRUMENTS/EQUIPMENT PURCHASED OUT OF/PROVIDED BY CSIR EXTRAMURAL RESRARCH FUND SHOULD CARRY THE LABEL "CSIR FUNDED".**

COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH
(EXTRAMURAL RESEARCH UNIT-II)

CSIR COMPLEX
Opp. Instt. Of Hotel Management
Library Avenue, Pusa,
New Delhi – 110 012

Dated:-26-09-2020

No.60(0117)/19/EMR-II

From:
Head, HRDG

To,
Dr. V.Sankar
Department of Pharmaceutics
PSG College of Pharmacy,
Coimbatore – 641004 (TN)

Sub: Renewal of grants for your scheme on "Mupirocin .....Infections"

Sir,
The Director-General, Scientific & Industrial Research has been pleased to sanction of the above scheme with the following grants for the period from 01-04-2020 to 31-03-2021.

	Amount	Details of staff	
(i) Staff:	Rs. 4,20,000/-	JRF/SRF/RA	One (SRF/JRF)
(ii) Contingency:	Rs. 4,00,000/-		
(iii) Equipment	Nil		
Total	Rs.8,20,000/-		

2. This grant is subject to the terms and conditions on which the scheme was originally sanctioned and as modified from time to time.
3. Bill in triplicate in enclosed proforma claiming grant sanctioned may please be sent through the appropriate authority of your institution after complying with the formalities required under the rules. The position regarding unspent balance of the previous year's grants must be clearly mentioned head-wise in the bill failing which it may be returned unpassed for compliance.
4. Particulars of staff working in the scheme i.e. his name, fellowship (JRF/SRF/RA) held, date of joining, resignation etc. for whom claim under head "Staff" is made should invariably be mentioned in the bill.
5. The expenditure is debatable to budget head "Special Research Programmed Extramural Research Grants" (Res. Schemes).

PS: Grants will be released on receipt of **Utilization Certificate and statement of accounts** which may please be Sent along with the claim & EFT Transaction Form. The grant will be sent through RBI-EFT (Electronic Funds Transfer).& **Subject to Date of Commencement of the scheme**

Yours faithfully,

30/09/2020

(R.S.D.RISHI)
SECTION OFFICER
अवर सचिव / Under Secretary
सी॰ एस॰ आई॰ आर॰-मानव संसाधन विकास समूह
CSIR-HRD Group
सीएसआईआर कॉम्प्लेक्स, पूसा, नई दिल्ली-12
CSIR Complex, Pusa, New Delhi-12

Copy to:
1. **Registrar, PSG College of Pharmacy,Coimbatore – 641004 (TN)**
2. **Director, CSIR-Institute of Genomics and integrative Biology, North Campus, Mall Road, Delhi – 110 007**

(iii) The statement of accounts duly audited by the Accounts Officer and counter-signed by the next higher authority in respect of grants received & expenditure incurred during previous year should be sent to this office with the bill claiming grants for the above period. (ii) Your attention is drawn to the rule No.03 of the Terms & Condition of CSIR Research Grant booklet.

FORM GFR 19-A
FORM OF UTILIZATION CERTIFICATION

Sl. No	Particulars	Letter No./Bank Transaction ID Nos. & Date	Amount
1.	Grants received form CSIR during the year (please provide details of all letters/bank transactions IDs with dates)	No 60(0117)/19/ EMR –II DT 17.07.19	4,73,333
2.	Unspent balance of previous year	NIL	NIL
3.	Interest earned/ accrued on CSIR grant		Rs.6,897
	Total		Rs.4,80,230

Certified that out of Rs.4,73,333./-..of grant-in-aid released by Extramural Research (EMR) Division of HRDG (CSIR) vide letter No./Bank Transaction ID Nos. 60(0117)/19/EMR –II DATED 17.07.2019 as given in the margin during the year..2019-2020 and Rs.6,897/-.earned/accrued as interest from bank on grants released by CSIR and Rs. ...NIL..on account of unspent balance of the previous year, a sum of Rs.1,32,650/-. has been utilized for the purpose for which it as sanctioned and that the balance of Rs...3,47,580/-remaining unutilized at the end of the year has been surrendered to EMR, HRDG (SCIR) (vide letter No. .....NIL....., DD/Cheque No.....dated.....)/**will be adjusted towards the grant –in-aid payable during the next year.**

2. Certified that I have satisfied myself that the conditions on which the grants-in-aid was sanctioned have been duly fulfilled/are being fulfilled and that I have exercised the following checks to see that the money was actually utilized for the purpose for which it was sanctioned. The detail expenditure incurred during the year is shown in the enclosed "Statement of Accounts (Receipt & Payment)".

Kinds of Checks exercised*

1. Vouchers and Statement of Accounts
2. Grant-in-Aid
3. Expenditure Register

For PSG COLLEGE OF PHARMACY

CHIEF FINANCE OFFICER

Signature of the Authorised Officer.....
Designation.....
Date 25.08.2020
Seal

V. VIMALA, B.Com., A.C.A.,
Chartered Accountant
Membership No : 37689

(Countersigning Authority)
Date 25.08.2020
Seal Dr. M. Ramanathan, M.Pharm, Ph.D.
Principal
PSG College of Pharmacy
Peelamedu, Coimbatore-4

The Utilization certificate and statement of account should be signed by Head of the Finance & Accounts and countersigned by Registrar/Dean/Director of the University/Institute.