JMBFS

Journal of Microbiology, Biotechnology and Food Sciences

International peer-reviewed scientific online journal

Published by Faculty of Biotechnology and Food Sciences

MICROWAVE AIDED SYNTHESIS OF ZINC OXIDE NANOCERAMICS: A POTENT BIOACTIVE AGENTS WITH THERAPEUTIC CHARACTERS

Vasanth Patil H.B[1,3], Mallikarjunaswamy C[2], Guru Kumar D[3*]*

Address(es): Vasanth Patil H.B

[1]Postgraduate Department of Bio-Technology, JSS College of Arts, Commerce and Science (Autonomous College of University of Mysore), Ooty Road, Mysuru- 570 025, Karnataka, INDIA.

[2]Postgraduate Department of Chemistry, JSS College of Arts, Commerce and Science and JSS Research Centre (A recognized research centre of University of Mysore), Mysuru-570025, Karnataka, India.

[3]Division of Biochemistry, School of Life Sciences, JSS Academy of Higher Education and Research, Mysuru, INDIA.

*Corresponding author: vasanth.patil09@gmail.com and gurukumard@jssuni.edu.in

https://doi.org/10.55251/jmbfs.9690

ARTICLE INFO

Received 6. 12. 2022
Revised 5. 4. 2024
Accepted 19. 4. 2024
Published 1. 6. 2024

Regular article

OPEN ACCESS

ABSTRACT

Nanoparticles have been inexhaustibly utilized in Nanochemistry cohere with Bio-Technology to upgrade the immobilization and movement of catalysts in pharmaceutical nanoengineering for conveyance of helpful specialists in incessant illness diagnostics and in sensors.Herein communication we report microwave irradiation technique implemented for the preparation of novel Zinc oxide nanoparticles with beneficial bio-efficacy wherein the method employed has the advantages of producing small particle size metal oxide with high purity owing to short reaction time. We successfully synthesized and characterized two Zinc oxide based Cs_2 doped ZnO_2 and Li_2 doped ZnO_2 nanoparticles and were subjected to *in vitro* free radical scavenging assay wherein all the particles could scavenge DPPH and Nitric oxide radicals with less IC_{50} value over the positive control. Microbicidal properties of nanoparticles were proved by its effectiveness against both Gram positive and Gram negative bacteria tested besides its action against *Candida albicans*. Both nanoparticles synthesized showed a prominent inhibition of erythrocyte lysis by PhospholipaseA2 in a concentration dependent manner indicating better anti-inflammatory agent with possibility of preventing cancer. In this study we demonstrate by shell less CAM assay that synthesized nanoparticles could inhibit *in vivo* angiogenesis which would otherwise under abnormal conditions causes the acceleration of several inflammatory diseases in spite of its role in normal growth and wound healing process. Inhibition of such process is the promising methodology to hinder the progression of diseases. Present characteristic features make use of ZnO_2 based doped nanoparticles to be a possible approach as a therapeutic molecule with favourable biological performance.

Keywords: Zinc oxide, Antioxidant, Anti-inflammatory, Anti-angiogenic, Antimicrobial, CAM-Chick Chorioallantoic membrane assay

INTRODUCTION

Nanoparticles have been copiously utilized in clinical Bio-Technology to upgrade the immobilization and action of catalysts **(Wang, 2006)** in pharmaceutical nanoengineering for conveyance of restorative operators **(Zhang et al., 2008)**, in inveterate infection diagnostics and in sensors and imaging strategies **(Hong et al., 2008)**. Nano oxide materials have found wide extending applications especially as catalysts and as beginning materials for making progressed auxiliary ceramics **(Kokila et al., 2008)**. Amid sintering and forming of oxidic materials are utilized for viable applications. Utilize of nano measured particles as beginning materials can be of awesome advantage since of the accessibility of huge surface regions compared to its bulk partner **(Anil Reddy, 2009)**.

A few strategies have been created for the planning of nanomaterial's **(Pramila et al., 2023)**; procedures like splash pyrolysis, warm decay, atomic bar epitaxy, and chemical vapor statement have been broadly utilized within the amalgamation of nanomaterial's, one such prepare is the work of microwave illumination strategy. Nanometric items moreover result when a vaporous reactant is utilized in microwave synthesis as watched within the arrangement of aluminum nitride by carbothermal lessening. Solvothermal microwave strategy has been depicted already for the arrangement of nanometric metal particles **(Rao et al., 2005)**. In any case, no common procedure has however been portrayed for the planning of nanomaterial's based on the use of microwaves. In this communication we report microwave light strategy for the planning of oxide nanoparticles. The strategy is based on a technique that's of exceptionally common appropriateness. The utilization of microwave illumination within the arrangement of nanoparticles is detailed in later a long time. Compared to the ordinary strategies, the microwave union has the focal points of creating little molecule estimate metal oxide with tall virtue owing to brief response time. It is found that this strategy is quick, mellow, vitality productive and environment neighborly course to create Zinc oxide nanoparticles.

Zinc oxide in expansion to different specialized applications (semiconductors), it is utilized in a arrangement of corrective preparates, sun security cream, skin break out treatment or as a wound dressing. Application of zinc oxide has been appeared to quicken the recuperating of both constant and intense wounds and it too shows antibacterial and anti-inflammatory conduct. ZnO_2 impact on epithelialization of wounds as well as its bacteriostatic property advances it as a topical wound dressing. It can be utilized in treatment of dermatitis, diaper rashes, diaper wipes, rankles, and open skin bruises **(Voicu et al., 2013)**.

The explore for new strategies to bargain with the illnesses causing microscopic organisms heighten as a result of resistance improvement by the pathogens against ordinary anti-microbial, Analysts have to be distinguish and create the another era of drugs or operators to control bacterial diseases. Antibacterial considers on natural materials are frequently not steady especially at tall temperatures and/or weights compared to inorganic antibacterial specialists **(Sawai et al., 2003)**. Reports are accessible on the impressive antibacterial action of inorganic metal oxides like TiO_2, MoO_3 **(Shivaganga et al., 2022)**, ZrO_2P_7, **(Deepakumari et al., 2022)** ZnO **(Mallikarjunaswamy et al.,2022)** SiO_2, MgO_2, NiO **(Mallikarjunaswamy et al., 2022)** CaO_2, BiOCl **(Mallikarjunaswamy et al., 2023)** CeO_2, $BiVO_4$ **(Pramila et al., 2020)** and ZnO_2 showing bacteriostatic, antimicrobial, or biocidal activity. Particularly, TiO_2, ZrO_2 **(Lakshmi et al., 2022)**, $MnWO_4$ **(Shivaganga et al., 2023)**, MgO_2, and CaO_2 are of specific concern since they are not as it were steady beneath cruel prepare conditions, but moreover are considered as secure materials to people **(Narayanan et al., 2012)**.

Besides, ZnO_2 shows up to successfully stand up to microorganisms **(Nagarajan & Vijayaraghavan, 2008)**. The reason for selecting ZnO_2 nanoparticles for the display think about is that it could be a metal oxide, which is much steadier and features a longer life than organic-based disinfectants and antimicrobial specialists **(Hewith et al., 2001)**. Zinc is additionally a basic constituent for cell development and in repressing bacterial proteins like dehydrogenase and certain defensive proteins such as thiolperoxidase and glutathione reductase **(Priyanka et al., 2009)**. In this study we have carried out antibacterial measure against four pathogenic microbes and an organism wherein Cesium and lithium doped ZnO_2 are strong against all the tried strains. Indeed in spite of the fact that meager reports are accessible with respect to antioxidant property of nanoceramics we tried for in vitro antioxidant capacity of doped ZnO_2 nanoparticles to rummage receptive free radicals and anti-inflammatory action was gotten to by Roundabout hemolytic test utilizing PLA_2 as a proinflammatory chemical and antiangiogenic test were moreover carried out utilizing shell less CAM (Chorioallantoic film) test to assess the viability of doped ZnO_2 nanoparticle which makes it to be a conceivable approach to utilize as restorative atom with positive natural exercises. Our objective is to synthesize Zinc oxide based nanoparticles doped with Cs_2 and Li_2, characterization of the same and its natural applications.

MATERIAL AND METHODS

Chemicals

All chemicals were purchased from Sisco Research Laboratories, Mumbai, India, and they were of analytical grade. Pathogenic Microorganisms were procured from Department of Molecular Biology, Yuvaraja's College, University of Mysore, Mysuru and were maintained in the laboratory in Mueller hinton agar slants which were subjected repeated sub culturing for every 8 days.

Chemistry

Synthesis of nanoparticles was carried out according to the method described previously by **Arunkumar et al., (2007)** with slight modification wherein the hydrated metal oxalate precursors were prepared by dissolving equimolar proportions of the respective metal salts (Zinc Oxalate and Lithium oxalate were used for Li_2ZnO_2 synthesis; Zinc Oxalate and Cesium oxalate for Cs_2ZnO_2 Synthesis) and oxalic acid in minimum volume of water and was stirred for about 15 min on a magnetic stirrer. The different metal salts show different coloured precipitate at different pH range of 2–6. The precipitates of respective metal oxalates were washed with cold distilled water till it was free from the respective sulphate and excess oxalic acid. Finally, the precipitate was washed repeatedly with dry acetone and then dried under vacuum and was transferred into a crucible and ignited in an electrical oven individually for partial decomposition. Then it was placed in a microwave oven synthesizer having frequency 5.0 GHz for about 0–30 min at various power levels 0–90. The solids burn by producing different coloured light depending upon the metal present in the carboxylate precursors and leaving behind respective metal oxides. The nano sized fillers so obtained were characterized by SEM, EDS, DLS and UV-Visible Spectral studies.

Biological assays for nanoparticles

Antioxidant assays

DPPH radical scavenging assay

The DPPH radical scavenging activity was performed using the methodology described by Scherer & Godoy (2009). In summary, distinct aliquots of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles independently, with concentrations ranging from 2–10µg/ml, were combined with 1 millilitre of DPPH solution (0.1 millilitres in 95% ethanol). As a negative control, DPPH alone was used in another reaction, and the combination was left to stand at room temperature for 20 minutes. The resulting solution's absorbance was measured at 517 nm using an HITACHI, U-2900 UV-VIS spectrophotometer. As a positive control, butylated hydroxyl toluene (BHT) was employed **(Vasanth et al., 2018)**. The mean values are computed after the experiment was run in triplicate. The sample concentration at which 50% of the DPPH radicals were scavenged is represented by the IC50 value, which is a measure of the radical scavenging potential. The following formula is used to calculate the absorbance at 517 nm, which is used to determine the radical scavenging ability: Scavenging effect (%) = [1- A of sample $_{(517nm)}$ / A of control $_{(517nm)}$] x 100

Nitric oxide scavenging assay

Sodium nitroprusside was converted to nitric oxide, which was then quantified using the Griess reagent. In an aqueous solution at physiological pH, sodium nitroprusside spontaneously produces nitric oxide **(Marcoci Etal 1994)**. This nitric oxide then combines with oxygen to produce nitrite ions, which are quantifiable using Griess reagent. Because nitric oxide scavengers compete with oxygen for available oxygen, nitric oxide synthesis is decreased. Different amounts of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles individually (2-10 µM/ml) were mixed with 1 ml of sodium nitroprusside (5 mM) in phosphate buffer saline (0.1M, Ph-7.4) and incubated at room temperature for 2 hours. Without the sample, a parallel reaction mixture was maintained as a control. Subsequently, 0.5 millilitres of Griess reagent containing 0.1% N-1-naphthyl ethylenediaminedihydrochloride, 2% H_3PO_4, and 1% sulphanilamide was added. A standard solution's absorbance was used to measure the absorbance of the chromophore created when nitrite was diazotized with sulphanilamide and then coupled with napthylethylene diamine. This absorbance was measured at 546 nm. The mean values are computed after the experiment was run in triplicate. The radical scavenging activity was calculated similarly as described earlier for DPPH radical scavenging assay.

Anti-inflammatory assay

Indirect hemolytic assay for PLA_2 inhibition

By utilising bovine serum albumin as a reference (0-75µg/ml), the protein concentration in the venom was determined using Lowry's technique. The method used was a semi-quantitative indirect hemolytic assay **(Boman and Kaletta, 1957)**. In short, a solution of egg yolk, packed human erythrocytes, and phosphate buffer saline (1:1:8 V/V) was made. Varespladib was employed as the usual medication, and a reaction mixture devoid of nanoparticles served as the control. One millilitre of this mixture was incubated with 20µg of enzyme primed with Cs_2ZnO_2 and Li_2ZnO_2 independently at varied concentrations (2, 4, 6, 8, 10 nM). After the reaction was halted after 10 minutes at 37 ^{0}C by adding 9 ml of ice-cold phosphate buffer saline, the mixture was centrifuged for 10 minutes at 6000 rpm. The amount of hemoglobin released by the action of PLA_2 in the supernatant was measured at 540 nm. Lysis of erythrocytes by adding 9 ml of distilled water to the control reaction mixture was taken as 100%. The experiment was carried out in triplicates and the mean values are calculated.

Anti Angiogenic activity

Chick Chorioallantoic membrane (CAM) assay

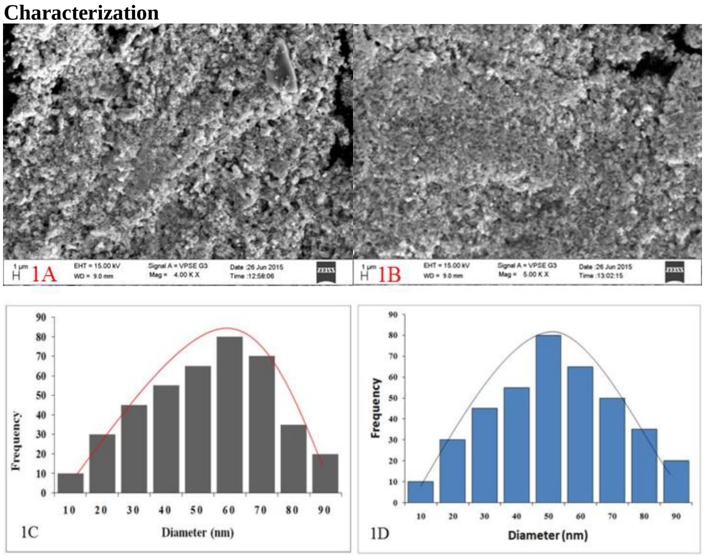
With a few changes, the CAM assay was performed using the previously published Chen et al. (2014) methodology. The fertilised chicken eggs were placed in a humidified incubator and incubated at 37 °C. After removing the egg shell on the eleventh day of development, the premature embryo was placed in a culture vial and saturated with 25 ng/ml of vascular endothelial growth factor (VEGF). Discs containing 10µg of each of the Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles were placed on the developing blood vessel, and the culture vials were sealed with sterile polymer wrap before being incubated for 48 hours at 37 °C in a humidified environment. We looked for variations in the microvessel density around the nanoparticle-saturated disc in the culture vials.

Antimicrobial activity (Disc diffusion method)

Antimicrobial activity was determined by disc diffusion method. Two Gram negative bacteria *Escherichia coli*, *Pseudomonas fluorescence* and two Gram positive bacteria *Micrococcus luteus, Bacillus subtilis* and a fungal culture *Candida albicans* were inoculated and maintained under aseptic condition in Mueller hinton broth and Sabouraud dextrose broth respectively for the assay. Culture media primed with agar was poured into sterile petriplates followed by Microbial swab was streaked on the medium for a lawn of growth for respective microbial culture. The sample discs containing different concentrations of doped ZnO_2 nano particles (5, 10, 20, 40 µg/ml) were placed on the surface of the agar medium at the correct distance apart using flamed sterilized forceps and a standard antibiotic of concentration 40µg/ml placed at centre and were incubate for 24hours at 37 ^{0}C. Zone of inhibition in diameter (mm) was measured. And minimum inhibitory concentration (MIC) was determined, where the lowest concentration of an antimicrobial agent that will inhibit the visible growth of a microorganisms.

RESULTS

Characterization



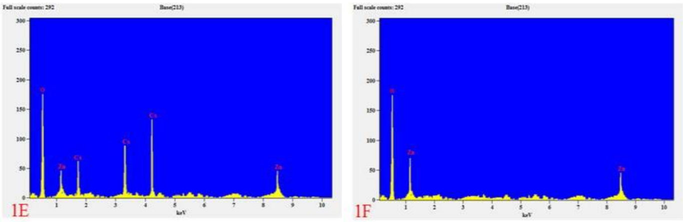


Figure 1 Physical Characterization of Cs_2ZnO_2 and Li_2ZnO_2 nano particle. 1A & 1B Scanning electron microscopy images; 1C &1D Dynamic light scattering; 1E & 1F Energy Dispersive X-ray spectral studies.

The domain size of the synthesized nano particles were assessed by SEM analysis (Figure 1A and 1B) and DLS measurements (Figure 1C and 1D),which reveals all the synthesized metallic particles are within upper threshold limit(100nm),with an average domain size of 60nm and 50nm for Cesium and Lithium Zincate respectively.

Furthermore, the success of green synthesis of Cs_2ZnO_2 and Li_2ZnO_2 nano particles affected by microwave irradiation technique was ascertained by Energy Dispersive X-ray spectral studies (Figure 1E and 1F). As can be seen from the figure, the cesium/lithium zincate nano particles show corresponding EDS peaks at different X-ray energies, owing to the difference in their binding potentials.

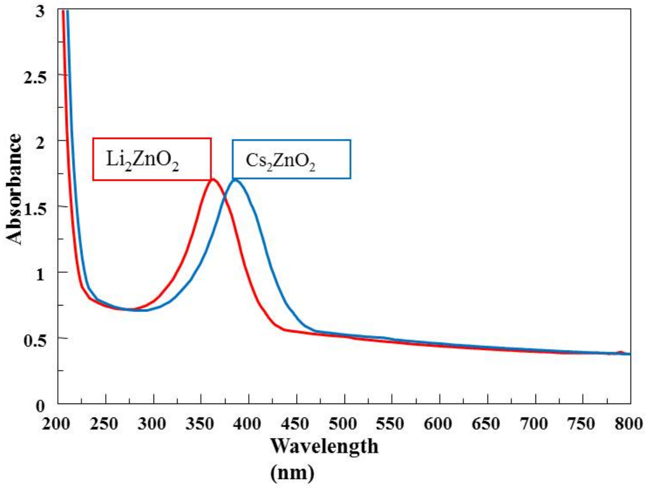


Figure 2 UV-Visible Spectrophotometric analysis of Cs_2ZnO_2 and Li_2ZnO_2

The synthesized nano particles were also subjected to UV-visible spectral studies to ascertain their optical absorption behaviors. The UV-visible spectrum of Cs_2ZnO_2 nano particles exhibit a broad shouldered 325-425 nm, however the integration of Cs_2 into the zinc lattice is found to red shift the UV absorption maximum towards higher wavelength regions.

Anti-Oxidant Assays

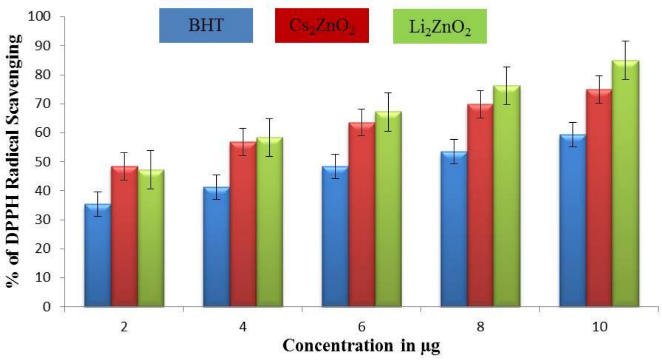


Figure 3 DPPH radical scavenging assay of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles

The experiment was carried out in triplicates and the results indicates Mean ± SE

Zinc oxide nanoparticles synthesized by microwave irradiation method were tested for *in vitro* antioxidant capacity, Out of which the percentage scavenging of DPPH was more in the presence of Li_2ZnO_2 nanoparticle with higher the IC_{50} value of 0.041 µ moles/ml; compared to that of positive control BHT with the IC_{50} value of 0.023µ moles/ml. And the scavenging capacity of Cs_2ZnO_2 increases in a concentration depended manner with the low IC_{50} value of 0.013 comparatively (Figure 3).

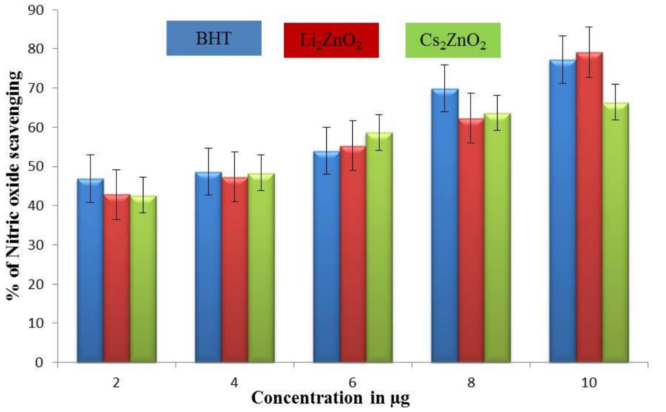


Figure 4 Nitric oxide radical scavenging assay of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles

The experiment was carried out in triplicates and the results indicates Mean ± SE

Nitric oxide radical scavenging was another method for *In vitro* antioxidant assay wherein Li_2ZnO_2 has almost same percentage of radical scavenging except at concentration of 2 and 8µg to that of positive control (Figure 4). Cs_2ZnO_2 showed high percentage of scavenging at the concentration of 6µg with lowest IC_{50} value compared to other positive control BHT (Table 1).

Table 1 IC_{50} value of ZnO_2 doped nanoparticles for Nitric oxide radical scavenging assay.

DRUG	BHT	Cs_2ZnO_2	Li_2ZnO_2
IC_{50} Value (µmoles/ml)	**0.023**	**0.016**	**0.051**

Anti Inflammatory Assay

Since the compounds showed positive results for antioxidant activities they were also examined for Anti Inflammatory activity (Indirect Haemolytic Assay) by using PLA2 an enzyme which usually causes hemolysis as a consequence of inflammatory reactions.

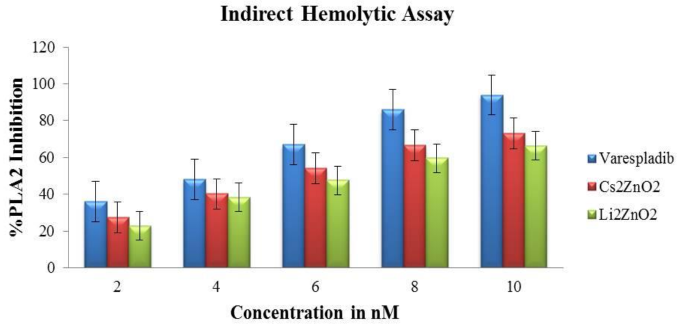


Figure 5 Indirect Hemolytic Assay of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles.

The experiment was carried out in triplicates and the results indicates Mean ± SE
The ability of the compound to prevent the hemolysis of RBC's indicates its Anti Inflammatory capacity wherein Cs_2ZnO_2 showed higher percentage of enzyme inhibition (Figure 5) in a concentration dependent manner with lowest IC_{50} value (Table 2).

Table 2 IC_{50} value of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles for Indirect hemolytic assay.

DRUG	Varespladib	Cs_2ZnO_2	Li_2ZnO_2
IC50 Value(nM)	**0.02**	**0.017**	**0.055**

Anti-Angiogenic Activity Assay

Nanoparticle based chemotherapeutic specialists are outlined such that they can latently or effectively target cancer cells. Shell less CAM test was performed to know the conceivable activity of ZnO_2 on angiogenesis wherein both Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles at the concentration of 10µg was utilized to immerse the circle in that it might repress the assist development of blood vessel within the locale where the nanoparticles were stacked (shown by arrows) compared to emptied spots passing on that it anticipates angiogenesis (Figure 6) by diminishing supplement supply to tumor cells as a result of diminish in microvessel thickness.

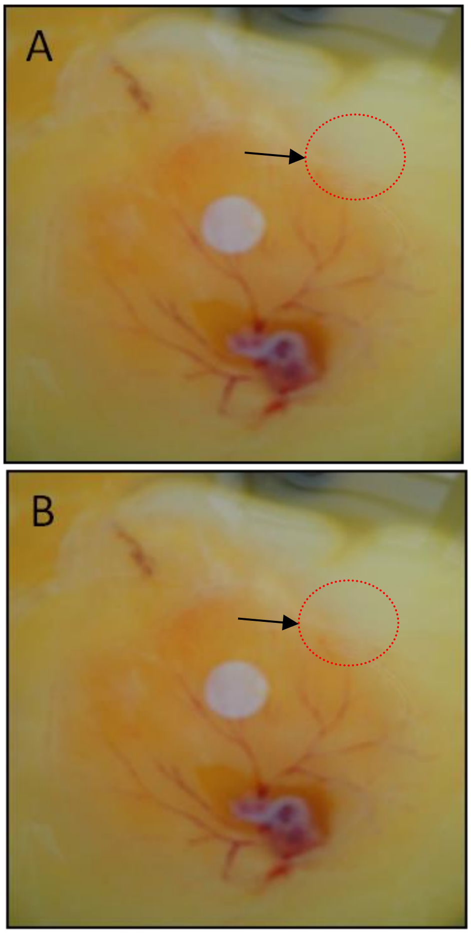


Figure 6 Shell less CAM assay for Anti-Anigiogenic property of Cs_2ZnO_2 (A) and Li_2ZnO_2 (B).

Anti microbial activity

The synthesized Cs_2ZnO_2 and Li_2ZnO_2 nano particles were screened for its antimicrobial activities against two Gram positive and two Gram negative bacteria including fungal pathogen *Candida albicans*. Invitro studies by disc diffusion method clearly shows the antimicrobial efficacies of the nanoparticles.

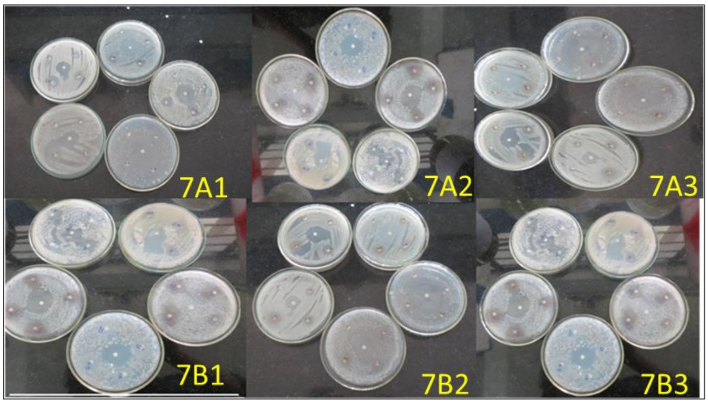


Figure 7 Invitro Antimicrobial activities of Cs_2ZnO_2 and Li_2ZnO_2. 7A1, 7A2, 7A3 were triplicates for Cs_2ZnO_2 nanoparticles and 7B1, 7B2, 7B3 were triplicates for Li_2ZnO_2 nanoparticles.

Table 3 Minimum Inhibitory Concentration values of Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles

	Escherichia coli	*Pseudomonas fluorescence*	*Bacillus subtilis*	*Micrococcus luteus*	*Candida albicans*
Gentamycin	6.1 µg/ml	7.02 µg/ml	5.35 µg/ml	4.16 µg/ml	--
Cs_2ZnO_2	7.32 µg/ml	8.21 µg/ml	7.55 µg/ml	7.82 µg/ml	6.12 µg/ml
Li_2ZnO_2	6.25 µg/ml	7.12 µg/ml	-----	5.82 µg/ml	5.12 µg/ml

DISCUSSION

Nanoparticles can be functionalized to carry and convey restorative operators such as drugs, qualities, or proteins. Lithium-doped zinc oxide nanoparticles have been examined as sedate conveyance vehicles due to their biocompatibility, controlled discharge properties, and potential for focused on conveyance to particular cells or tissues. Nanoparticles can act as differentiate specialists in different imaging modalities, counting fluorescence imaging, attractive reverberation imaging (MRI), and computed tomography (CT). Helpful parts for zinc in numerous infections have been built up in later a long time. ZnO_2 contains a exceptionally great potential to move into the clinic **(Shopsin et al., 1999)**. The improvement of builds to diminish oxidative harm caused by free radicals in natural substances with more prominent productivity can be accomplished by mixing of fabric science with Bio-Nanotechnology **(Kannan & Hyun 2013)**. Lithium-doped zinc oxide nanoparticles have been investigated as imaging specialists due to their fluorescence properties, biocompatibility, and potential for focused on imaging of particular tissues or cellular structures **(Marco et al., 2020)**. In this examination such sort of builds were made and were tried for in vitro antioxidant tests which shows the capacity of nano ZnO2 to give electrons and in this way extinguishing steady free radical like DPPH and was able compete with oxygen driving to decreased generation of nitric oxide (NO) which was assessed utilizing Griess reagent. Upon rummaging DPPH Li_2ZnO_2 appeared maximum percentage (80% at the concentration of 10 µg/ml) of rummaging with comparatively higher concentration required to induce 50% restraint (Figure 3). Li_2ZnO_2 has practically equivalent to capacity in decreasing the generation of nitric oxide by 80% at 10µg/ml concentration (Figure 4) with shifting IC_{50} esteem (Table 1). In spite of the fact that NO is utilized by the antigen handling cells like macrophages upon incitement by administrative flag particles called interleukins and intergalactic to guard against pathogens its overabundance action amid typical condition; it acts as a receptive radical, specifically harms typical tissues. Assist, nitric oxide can too respond with superoxide anion radical to create an indeed more grounded oxidant peroxy nitrite **(Lau et al., 1999)**. In this way ZnO_2 nanoparticles might proficiently rummage these responsive atoms which may diminishes oxidative harm to typical cells and have to be be tried in vivo. NO created peroxynitrite by responding with superoxide anion. Peroxynitrite, as a capable oxidant, can either specifically connected with or oxidize different kinases and translation components, subsequently irritating the cellular signaling organize and advancing inflammation-driven cellular change **(Joydeb & Youthful 2012)**.

Inflammation have defense component, is an quick reaction of the body to tissue damage caused by microbial contamination and other harmful boosts **(Joydeb & Youthful 2012)**. Aggravation when hoisted leads to a few disarranges of which cancer is the extreme result. Aggravation was primarily caused by the action of Lipoxygenase (LOX) and Cycloxygenase (COX) which depends on the accessibility of arachidonic corrosive as a substrate. This substrate was determined from phosphotidyl choline by the activity of Phospholipase A2 (PLA_2) which acts as a source of irritation. Restraint of PLA_2 chemical by endogenous inhibitors, common compounds is of potential restorative pertinence in numerous provocative illness states. The presence of diverse sorts of PLA_2 in incendiary illnesses drew consideration to the significance of finding the particular and particular inhibitors for the chemical **(Rekha et al., 2014)**. Lithium and cesium-doped zinc oxides have appeared promising anti-inflammatory properties, which can be advantageous within the treatment of provocative clutters. These materials have the potential to tweak safe reactions and diminish aggravation, making them appropriate candidates for the improvement of medicate conveyance frameworks and anti-inflammatory treatments **(Sauvik et al., 2022)**. Comparable comes about are gotten by both Cs_2ZnO_2 and Li_2ZnO_2 integrated by microwave light strategy wherein Cs_2ZnO_2 displayed promising result by restraining PLA_2 action up to 70% (Figure 5) indeed at moo concentration of 10nM comparatively (Table 2) there by diminishing incendiary reaction.

It is well known that irritation is exasperated by ROS generation, in which ROS act as auxiliary delivery people in signaling and acceptance of proinflammatory go betweens. Expanded levels of free radical NO by proinflammatory inducible nitric oxide synthase (iNOS) contribute to incessant irritation. Nanoceria managed as a nanotherapeutic treatment smothers the expression of iNOS and diminishes NO generation in J774A.1 murine macrophages as well as extinguishes ROS generation.
Fiery reactions play conclusive parts at diverse stages of tumor advancement, counting start, advancement, harmful change, intrusion, and metastasis **(Sergei et al., 2010)**. For all of these forms it needs the supply of supplements through the arrangement of unused blood vessels by a handle of angiogenesis which is being a complex prepare, including different quality items communicated by diverse cell sorts leads to tumor improvement beneath extraordinary conditions **(Sangiliyandi et al., 2009)**. Tumor advancement initiated by irritation may happen early or late in tumor improvement and can lead to actuation of premalignant injuries that were torpid for numerous a long times. The aggravation advances tumor advancement by means of various instruments and, in expansion to upgraded survival, can moreover include the so-called angiogenic switch, which permits a small torpid tumor to get the blood supply vital for the development phase **(Lewis & Pollard, 2006)**. Preventing this stage may be distant better or improved distant better target for tumor control by nanocomposites.
With suitable surface alterations Metalic and non-metalic Nanomaterials counting liposomes, polymeric nanoparticles, carbon nanotubes, nanowires, viral nanoparticles and cross breeds, quantum specks and dendrimers are right now being proposed, as devices for sedate conveyance, imaging and in cancer treatment and conclusion **(Sangiliyandi et al., 2009)**, wetheories that doped metal oxides seem moreover work so also and tentatively demonstrated the antiangiogenic impact of Cs_2ZnO_2 and Li_2ZnO_2 by CAM measure wherein the development hindered microvessel can be watched within the culture vials contained untimely chick developing life stacked with the nanoparticles compared to emptied spots (Figure 6) showing tumor smothering property by means of the blockage of unused blood vessel arrangement. Cesium-doped zinc oxide nanoparticles can be utilized in cancer treatment approaches such as photothermal treatment (PTT) and radiation treatment. These nanoparticles can retain light or radiation vitality and change over it into warm, driving to localized hyperthermia or improved radiation impacts on cancer cells. Combination of anti-inflammatory approaches that target the tumor microenvironment with more advanced and specific tumoricidal drugs are required for the particular killing/control of cancer which would something else leads to progressed and regularly recalcitrant malady condition.
The results of antimicrobial considers confirms the bactericidal and fungicidal property of doped ZnO_2 nanoparticles (Table 3). The gotten comes about back the expanded surface range of Cesium/lithium zincate nano particles (Figure 1) affirmed by physical characterization that accounts for their expanded anti-microbial efficacies (Figure 7). The antimicrobial instrument of ZnO_2 nanoparticles would be primarily due to physical blockage by transport channels and harm the cell layer of pathogenic microbes due to scraped spot **(Lingling et al., 2010)**. In any case, the movement dependes on the bigger surface zone and concentration of ZnO_2 nanoparticles, whereas the crystalline structure and molecule shape would bring a small impact on its antimicrobial action **(Narayanan et al., 2012)**. Cs_2ZnO_2 nanoparticles have displayed antibacterial properties against different pathogens. They can be utilized in antimicrobial coatings **(Essia et al., 2022)**, wound dressings **(Rong et al., 2021)**, or disinfectant details to combat bacterial contaminations and advance recuperating.

CONCLUSION

The present study clearly indicated that Cs_2ZnO_2 and Li_2ZnO_2 nanoparticles would serve as a safe nano oxide form of Zinc and can be used as valuable therapeutic agents because of their extensive pharmaceutical properties which especially works as anti-inflammatory agents which intern prevents the tumor development and as a microbicidal could be used to overcome resistance development by pathogens. It's important to note that the use of these doped zinc oxide nanoparticles in medicine is still at the research stage, and their translation to clinical applications requires further investigation and validation. Additionally, the specific applications and efficacy may vary depending on factors such as nanoparticle properties, formulation, and targeted biological systems.

Acknowledgments: Authors are thankful to University Grant Commission, New Delhi (UGC-MRP: 1491-MRP/14-15/KAMY013/UGC-SWRO) for extending the funds to carryout this research work. And JSS Mahavidhya Peetha for the facilities and amminities provided.

REFERENCES

Anil Reddy, (2009). Preparation and Characterization of Iron Oxide Nanoparticles on Disaccharide Templates. *Journal of Pharmaceutical Research and Health Care*, *1*(2), 172-183. http://dx.doi.org/10.18311/ajprhc/2009/627

Arunkumar Lagashettya, Vijayanand Havanoorb, S., Basavarajab, S.D., Balajib, A., Venkataramanb. (2007). Microwave-assisted route for synthesis of nanosized metal oxides. *Science and Technology of Advanced Materials*, 8, 484-493. http://dx.doi.org/10.1016/j.stam.2007.07.001

Boman, H. G., & Kaletta. (1957). Chromatography of rattle snake venom. A separation of three phosphodiestrases. Biochimica et Biophysica Acta, 24, 619-631.

Chen, Z., Zhang, Y., et al. (2014). mTORC1/2 targeted by n-3 polyunsaturated fatty acids in the prevention of mammary tumorigenesis and tumor progression. *Oncogene, 33*(37), 4548-4557. http://dx.doi.org/10.1038/onc.2013/402

Deepakumari, H.N., Lakshmi Ranganatha, V., Nagaraju, G., Prakruthi, R., Mallikarjunaswamy, C. (2022). Facile green synthesis of zirconium phosphate nanoparticles using Aegle marmelos: antimicrobial and photodegradation studies. *Materials Today: Proceedings*. 62, 5167-5173. https://doi.org/10.1016/j.matpr.2022.02.579

Essia Hannachi, Firdos Alam Khan,Yassine Slimani, Suriya Rehman, Zayneb Trabelsi, Sultan Akhtar & Ebtesam A. Suhaimi, (2022). In Vitro Antimicrobial and Anticancer Peculiarities of Ytterbium and Cerium Co-Doped Zinc Oxide Nanoparticles. *Biology*, 11(12), 1-18. https://doi.org/10.3390/biology11121836

Hewitt, C. J., Bellara, S. T., Andreani, A., Nebe-von-Caron, G., Mcfarlane, S. T. (2001). An evaluation of the antibacterial action of ceramic powder slurries using multiparameter flow cytometry. *Biotechnological Letters*, *23*, 667-675. http://dx.doi.org/10.7508/nmj/2016/02/0077

Hong, B., Kai, J., Ren, Y., Han, J., Zou, Z., Ahn, C.H. (2008). Highly sensitive rapid, reliable, and automatic cardiovascular disease diagnosis with nanoparticle fluorescence enhancer and MEMS. *Advances in Experimental Medicine and Biology*, *614*, 265–273. http://dx.doi.org/10.1007/978-0-387-74911-2_30

Joydeb Kumar Kundu & Young-Joon Surh. (2012). Emerging avenues linking inflammation and cancer. *Free Radical Biology and Medicine, 52*, 2013-2037. http://dx.doi.org/10.1021/bi026262q

Kannan Badri Narayanan, Hyun Ho Park. (2013). Pleiotropic functions of antioxidant nanoparticles for longevity and medicine. *Advances in Colloid and Interface Science, 201*, 30-42. http://dx.doi.org/10.1016/j.cis.2013.10.008

Kokila, G.N., Mallikarjunaswamy, C., Lakshmi Ranganatha, V. (2022). A review on synthesis and applications of versatile nanomaterials. *Inorganic and Nano-Metal Chemistry.* 1-30. https://doi.org/10.1080/24701556.2022.2081189

Lakshmi Ranganatha, V., Nagaraju, G., Vidya, J.S., Deepakumari, H.N., Gurudutt, D.M., Mallikarjunaswamy, C. (2022). Indian bael mediated eco-friendly synthesis and performance evaluation of zirconium oxide nanoparticles: an efficient anti-microbial agent. *Materials Today: Proceedings*. 62, 5067-5070. https://doi.org/10.1016/j.matpr.2022.02.407

Lau, K. Y., Mayr, A., Cheung, K. K. (1999). Synthesis of transition metal isocyanide complexes containing hydrogen bonding sites in peripheral locations. *Inorganica Chimica Acta*, *285*, 223-232.

Lewis, C.E., & Pollard, J.W. (2006). Distinct Role of Macrophages in Different Tumor Microenvironments. Cancer Research, *66*(2), 605-612. http://dx.doi.org/10.1158/0008-5472

Lingling, Z., Yunhong, J., Yulong, D., Nikolaos, D., Lars, J., Malcolm, P. (2010). Mechanistic investigation into antibacterial behaviour of suspensions of ZnO nanoparticles against *E. coli*. *Journal of Nanoparticle Research*, *12*, 1625-1636. http://dx.doi.org/10.1007/s11051-009-9711-1

Parameswara, P., Pramila, S., Lakshmi Ranganatha, V. (2022) Green and facile synthesis of zinc oxide nanoparticles for enhanced photocatalytic organic pollutant degradation. *Journal of Materials Science: Materials in Electronics*. 33(25), 20361-20372. https://doi.org/10.1007/s10854-022-08852-z

Mallikarjunaswamy, C., Deepakumari, H.N., Nagaraju, G., Khosla, A., Manjunatha, C. (2022). Eco-friendly green synthesis, characterizations, and antimicrobial activities of nickel oxide nanoparticles. *ECS Transactions.* 107, 16303. https://iopscience.iop.org/article/10.1149/10701.16303ecst

Mallikarjunaswamy, C., Pramila, S., Shivaganga, G.S., Deepakumari, H.N., Prakruthi, R., Nagaraju, G., Parameswara, P., Lakshmi Ranganatha, V. (2023). Facile synthesis of multifunctional bismuth oxychloride nanoparticles for photocatalysis and antimicrobial test. 290, 116323. https://doi.org/10.1016/j.mseb.2023.116323

Marco Carofiglio, Sugata Barui, Valentina Cauda & Marco Laurenti, (2020). Doped Zinc Oxide Nanoparticles: Synthesis, Characterization and Potential Use in Nanomedicine. *Applied Sciences*, 10(5194), 1-43. https://doi.org/10.3390/app10155194

Nagarajan, P., & Vijayaraghavan, R. (2008). Enhanced bioactivity of ZnO nps—an antimicrobial study. *Science and Technology of Advanced Materials*, *9*, 1-7. http://dx.doi.org/10.1088/1468-6996/9/3/035004

Narayanan, P.M., Wijo Samuel Wilson, Ashish Thomas Abraham, Murugan Sevanan. (2012). Synthesis, Characterization, and Antimicrobial Activity of Zinc Oxide Nanoparticles Against Human Pathogens. *BioNanoScience*, *2*(4), 329-335. http://dx.doi.org/10.1007/s12668-012-0061-6

Pramila, S., Nagaraju, G., Mallikarjunaswamy, C., Latha, K.C., Chandan, S., Ramu, R., Rashmi, V., Ranganatha, V.L. (2020). Green Synthesis of BiVO4 Nanoparticles by Microwave Method using Aegle marmelos Juice as a Fuel: Photocatalytic and Antimicrobial Study. *Analytical Chemistry Letters*, 10(3), 298-306. https://doi.org/10.1080/22297928.2020.1785935.

Pramila, S., Ranganatha, V.L., Nagaraju, G., Mallikarjunaswamy, C. (2020). Microwave and combustion methods: a comparative study of synthesis, characterization, and applications of NiO nanoparticles. *Inorganic and Nano-Metal Chemistry*. 56(6), 527-538. https://doi.org/10.1080/24701556.2022.2081188

Priyanka, G., Brian, P., David, B. W., Wenjie, H., William, J. P., Anne, A.J. (2009). Antimicrobial activities of commercial nanoparticle against an environmental soil microbe, *Pseudomonas putida* KT2440. *Journal of Biological Engineering*, *3*(9), 1-13. http://dx.doi.org/10.1186/1754-1611-**3-9**

Rao, K.J., Krishnamurthy Mahesh, Sundeep Kumar. (2005). A strategic approach for preparation of oxide nanomaterials. *Bullentin of Material Science*, *28*(1), 19-24. http://dx.doi.org/10.1007/BF02711166

Rekha, N.D., Gowda, T.V., Aradhya, S.M., Suresha, R.N., & Jayashree, K. (2014). Anti-Inflammatory Properties of Memecylaene: A Novel Compound Isolated from *Memecylon malabaricum*. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*. *5*(2):1645-1654.

Rong Wei, Zhaowenbin Zhang, Min Xing, Yanling Zhou, Jiang Chang, (2021). Preparation and in vitro evaluation of Lithium-doped bioactive glasses for wound healing with nerve repair potential. Materials Letters, 292, 1-20. https://doi.org/10.1016/j.matlet.2021.129629

Sangiliyandi Gurunathan, Kyung-Jin Lee, Kalimuthu Kalishwaralal, Sardarpasha Sheikpranbabu Ramanathan Vaidyanathan, Soo Hyun Eomb. (2009). Antiangiogenic properties of silver nanoparticles. *Biomaterials*, *30*, 6341-6350. http://dx.doi.org/10.1016/j.biomaterials.2009.08.008

Sauvik Rahaa & Ahmaruzzaman, (2022). ZnO nanostructured materials and their potential applications: progress, challenges and perspectives. *Nanoscale Advances*, 4, 1868–1925. https://doi.org/10.1039/D1NA00880C

Sawai, J, Shoji, S, Igarashi H, Ashastimato A, Kokugan T, Shimizu M, et al. (2003). Quantitative evaluation of antibacterial activities of metallic oxide powders (ZnO, MgO, CaO) by conductimetric assay. Journal of Microbiological Methods, 54:177–182. http://dx.doi.org/10.1016/S0167-7012(03)00037-X

Scherer, R., & Godoy, H.T. (2009). Antioxidant activity index (AAI) by 2, 2-diphenyl-1-picrylhydrazyl method. *Food Chemistry*. *112*, 654-658. http://dx.doi.org/10.1016/j.foodchem.2008.06.026

Sergei, I., Grivennikov, Florian, R., Greten, & Michael Karin. (2010). Immunity, Inflammation, and Cancer, *Cell*, *140*, 883-899. http://dx.doi.org/10.1016/j.cell.2010.01.025

Shivaganga, G.S., Lakshmi Ranganatha, V., Mallikarjunaswamy, C., Sunil Kumar, K.C., Nagaraju, G., Parameswara, P. (2023). Biogenic synthesis of orthorhombic α-MoO3 nanoparticles for photocatalytic degradation and electrochemical sensing. *Journal of Materials Science: Materials in Electronics*. 34, 2226. https://doi.org/10.1007/s10854-023-11611-3

Shivaganga, G.S., Parameswara, P., Mallikarjunaswamy, C., Sunil Kumar, K.C., Soundarya T.L., Nagaraju, G., Punith, S., Lakshmi Ranganatha, V. Green, nonchemical route for the synthesis of MnWO4 nanostructures, evaluation of their photocatalytic and electrochemical performance. (2023). *Journal of Materials Science: Materials in Electronics*. 34(25), 1791. https://doi.org/10.1007/s10854-023-11190-3

Shopsin B., Gomez M., Montgomery S.O., Smith D.H., Waddington M., Dodge D.E., Bost D.A., Riehman M., Naidich S., Krieswirth B.N. (1999). Evaluation of protein A gene polymorphic region DNA sequencing for typing of *Staphylococcus aureus* strains. *Journal of Clinical Microbiology*, *37*, 3556-3563.

Vasanth Patil, H.B., Lakshmi Ranganatha, V., Prashanth, T., Mallikarjunaswamy, C. Synthesis and Biological Applications of (E)-N-Benzylidene-5-bromo-2-chloropyrimidin-4-amine Derivatives. (2018). *Asian Journal of Organic & Medicinal Chemistry*. 3, 10-13. 10.14233/ajomc.2018.AJOMC-P89

Vinutha, S.A., Meghashree, A.M., Gurudutt, D.M., Deeksha, S. K., Sunil Kumar, K. C., Karthik, G., Arun Kumar, N., Lakshmi Ranganatha, V., Parameswara, P., Mallikarjunaswamy, C. (2023). Facile green synthesis of cerium oxide nanoparticles using Jacaranda mimosifolia leaf extract and evaluation of their antibacterial and photodegradation activity. *Materials Today: Proceedings*. 89, 105-112. https://doi.org/10.1016/j.matpr.2023.05.592

Voicu, G., Oprea, O., Vasile, B.S., Andronescu, E. (2013). Antibacterial Activity of Zinc Oxide-Gentamicin Hybrid material. *Digest Journal of Nanomaterials and Biostructures*. *8*(3), 1191-1203.

Wang, P. (2006). Nanoscale biocatalyst systems. *Current Opinion in Biotechnology, 17*, 574–579. http://dx.doi.org/10.1016/j.copbio.2006.10.009

Zhang, L., Gu F.X., Chan, J.M., Wang, A.Z., Langer, R.S., & Farokhzad, O.C. (2008). Nanoparticles in medicine: therapeutic applications and developments. *Clinical Pharmacology and Therapeutics*, 83, 761–769. http://dx.doi.org/10.1038/sj.clpt.6100400