

CURRICULUM VITAE

Personal details



Name : Dasari Ramakrishna
Father's Name : D.Ashok
Date of Birth : 28 April 1983
Gender : Male
Nationality : Indian
Marital status : unmarried
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Education and Training:

Academic Profile: Ph.D in Applied Biology from CSIR-Indian Institute of Chemical Technology, Hyderabad, India.

Doctoral Advisor: Dr.Sunil Misra Principal scientist ,Toxicology Unit Applied Biology Division, CSIR-Indian Institute of Chemical Technology (IICT), Hyderabad, Telangana, India 500007.

Thesis title: “Evaluation of *in-vitro* and *in-vivo* genotoxicity effects of zoledronic acid - a bisphosphonate drug used for the treatment of bone cancer”.

Academic qualifications:

Course	Board/University	Division	%
10th (1998)	Central Board of Secondary Education	First	71.4 %
Intermediate (2000)	Board of Intermediate Education,OU	First	68.1 %
Graduation B.Sc (Microbiology, Botany,Chemistry) (2004)	Osmania University Hyderabad,Telangana India	First	77 %
Postgraduation M.Sc (AnimalBiotechnology) (2006)	University of Hyderabad, Hyderabad,Telangana, India	First	75%
Ph.D Applied Biology (2019)	CSIR-Indian Institute of Chemical Technology Hyderabad, Telangana,India	First	75%

Projects:

M.Sc dissertation:

As part of our course curriculum I have done a project under the supervision of **Prof Aparna Dutta Gupta Dept of Animal Sciences, University of Hyderabad:** - Project Title “Isolation and purification of cry-toxins (cry-A, cry-B, cry-AB, cry1-Ac) and its immunological studies. 2005-06

Industrial experience:

Project entitled “*In silico* design of dual inhibitors of Cyclooxygenase-2 and Lipoxygenase-5 using structure-based Pharmacophore modeling, virtual screening and docking studies” at GVK BIOSCIENCES, Hyderabad. 2009-10

Worked as a curator and have experience in curating clinical trials, ASCO, NCT and Pubmed journals with information regarding drug intervention with a particular application

like efficacy, diagnosis, prognosis, safety and toxicity from the science databases like pubmed, science direct, and NCI, also have hands on toxicology standardization using MedDRA Version 10.0.

2009-10

Professional certificate:

Received **professional training level II** in Protein modeling & rational drug design certified by Accelrys conducted at biocampus, Hyderabad, India

2009-10

Laboratory skills and practical experience:

- ◀ **Microbiological techniques:** Isolation, maintenance of pure cultures growth curve, coli form test, MIC test, serial dilution technique, antibiotic disc-sensitivity assay, biochemical tests for characterization of microorganisms and microscopy.
- ◀ **Electrophoretic techniques:** SDS-PAGE, Agarose gel electrophoresis.
- ◀ **Molecular biology techniques:** genomic DNA Isolation, plasmid DNA isolation, restriction mapping, molecular cloning, heterologous gene expression, PCR, western blotting & southern blotting.
- ◀ **Protein & Enzyme studies:** Protein estimation (Biuret, Bradford and Lowry) & protein purification.
- ◀ **Biophysical techniques:** Spectroscopy (UV, visible) Centrifugation, Titrations (pH metry etc).
- ◀ **Immunological techniques:** ELISA, Differential leukocyte count, blood platelet count, widal test, blood typing, purification of Ig-G, western blot etc.
- ◀ **Chromatographic techniques:** Paper chromatography, affinity Chromatography, thin layer chromatography, gel filtration, HPLC, atomic absorption spectroscopy.
- ◀ **Bioinformatics and computational biology:** Protein modeling & rational drug design molecular modeling, homology modeling, structure based drug design, analog based drug design & pharmacophore analysis.

Toxicity-tests: *in-vitro* and *in-vivo* genotoxicity studies.

- ◆ Maintenance and propagation of various established cell lines as per GLP compliance for toxicology studies.
- ◆ Carrying out core standard battery studies of toxicology in accordance with OECD GLP norms.
- ◆ Preparation, staining and microscopic analysis of mitotic metaphase spreads for structural chromosomal aberrations like breaks, gaps, minutes, translocation & pulverization (karyotyping).
- ◆ preparation of microscopic slides for observing spermatogonial, diakinesis for atypical bivalents autosomal asynapsis ,X-Y asynapsis ,trivalents/tetravalents in meiotic cells of germline cells
- ◆ Evaluation of micronuclei formation from PCE derived from bone marrow and peripheral blood cells of mammalian cells & comet assay.

List of publications:

- ❖ **Dasari, R.**, Misra, S. Zoledronic acid induces cytogenetic toxicity in male germline cells of Swiss albino mice. Drug and chemical toxicology (2018). 1-7.
- ❖ Bollu, V. S., Nethi, S. K., **Dasari, R. K.**, Rao, S. S. N., Misra, S., & Patra, C. R. Evaluation of in vivo cytogenetic toxicity of europium hydroxide nanorods (EHNs) in male and female Swiss albino mice. Nanotoxicology.2016; 10(4) 413-425.
- ❖ Porel, S., **Ramakrishna, D.**, Hariprasad, E., Gupta, A. D., & Radhakrishnan, T. P. Polymer thin film with in situ synthesized silver nanoparticles as a potent reusable bactericide. Current Science (Bangalore). 2011; 101(7), 927-934.

List of patents:

- ❖ T. P. Radhakrishnan, Shatabdi Porel, Aparna Dutta Gupta, **D. Ramakrishna**, “Nanoparticle embedded polymer film for antibacterial application”, Indian Patent No.296215 (Application No.: 2182/DEL/2007; Date of filing: 18/10/2007; Date of Grant: 26/04/2018).

Computational skills:

I have under gone with the following computer applications.

- 📁 computer fundamentals with MS. Office
- 📁 **Operating systems:** MS DOS, MS. Windows 98, 2000, Me, Xp.
- 📁 Acquaintance with the use of accelrys discovery studio 2.0 versions in molecular modeling techniques, protein sequence analysis and modeling, structure/target based drug design, analog based drug design, drug design based on pharmacophore analysis and drug design based QSAR

National/international conferences / workshops & seminars participated/attended:

- **Participated** in Poster session of the seminar on BIOVISION-2001 conducted by Aurora's degree college Osmania University - Hyderabad.
- Attended in both Poster and Paper presentation sessions of **National Level symposium** on occasion of 50 years of DNA (2003) – Hyderabad.

Attended Indo-German sci-tech forum: 2004:

Jointly conducted by University of Hyderabad and by German universities .

- ❖ Workshop on **plant biochemistry and biotechnology.**
- ❖ Workshop on **environmental research and technologies.**
- ❖ Workshop on **nanotechnology .**
- ❖ Workshop on **Molecular biology of infectious diseases.**

Awards & Fellowships:

- ◆ Awarded Junior Research Fellowship (**JRF**), (2011-2013) by Council of Scientific and Industrial Research (CSIR), New Delhi, India.
- ◆ Awarded Senior Research Fellowship (**SRF**), (2013-2016) by Council of Scientific and Industrial Research (CSIR), New Delhi, India.
- ◆ Awarded NET LECTURESHIP in **LIFESCIENCES** held on 20-12-2009.
- ◆ Selected for training programme conducted by GVKBIO, Hyderabad in Proteomics and Rational drug designing.
- ◆ Awarded NET LECTURESHIP (LS-NET) in **LIFESCIENCES** held on 18.06.2006
- ◆ Scored 83.54 percentile in Graduate Aptitude Test in Engineering (**GATE**)-February-2005 with 1089 all India rank.
- ◆ Secured state 7th rank in M.Sc common entrance test conducted by Osmania University Andhra pradesh.
- ◆ Selected for M.Sc Animal Sciences in the main list conducted by University of Hyderabad, through national level eligibility entrance test-**2004**.
- ◆ Selected for M.Sc Plant Sciences in the main list conducted by University of Hyderabad, through national level eligibility entrance test-**2004**.
- ◆ Selected for M.Sc Biotechnology Programme conducted by J.N.U through national level eligibility entrance test -**2004**.

References:

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email :smisra@iict.res.in.

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Declaration:

I hereby declare that information given in curriculum vitae is complete and accurate in every respect. I understand that any falsification or misrepresentation of information will be grounds for terminating consideration of my request.

Thanking you,

Date: 28/04/2021

Place Hyderabad

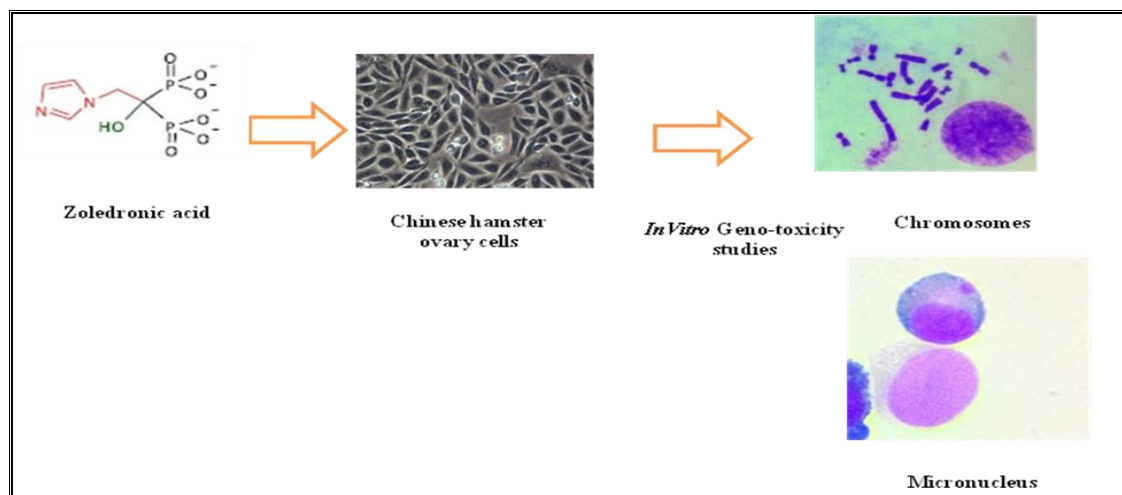
Regards

Dasari Rama Krishna

Doctoral Research summary

1a Evaluation of *in vitro* cytogenetic toxicity induced by Zoledronic acid.

The experiments of *in vitro* was designed in order to evaluate cytogenetic toxicity due to effect of Zoledronic acid. Cytogenetic toxicity potential was studied *in vitro* on Chinese Hamster Ovary (CHO) cells at a dose range of (50 μ M, 100 μ M and 200 μ M) ZA using the endpoints such as Chromosomal aberration test (CA), Mitotic index (MI) and Micronucleus (MN) test.

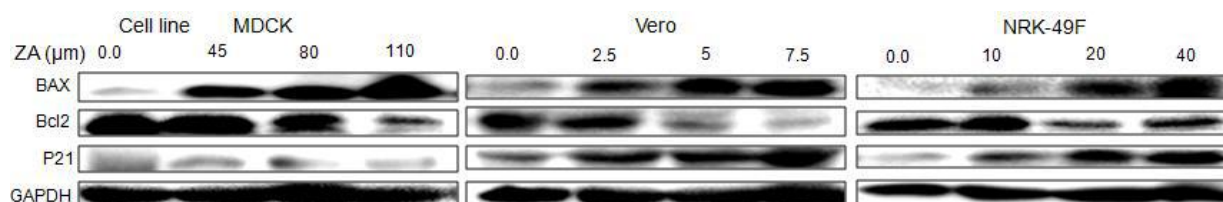


Scheme 1: Evaluation of *in vitro* cytogenetic toxicity induced by Zoledronic acid.

The results of chromosome aberration test performed reveal that there was a significant difference between positive controls and negative control for frequencies of chromatid breaks and polyploidy ($P < 0.001$). However in the treatment dose range of ZA 50 μ M, 100 μ M and 200 μ M, the percentage of aberrant metaphases, the percentage of aberration both (excluding and including gaps) remained non significant for all the dose range of ZA tested. There was a decrease in the mitotic index as a function of increase of dose that was significant (for all comparisons P -values were less than 0.01). In the MN, there was a significant ($P < 0.01$) induction of MN at a dose of 200 μ M which is the high among the doses of ZA tested. The overall representation of cytogenetic toxicity study of ZA is demonstrated in **Scheme 1**.

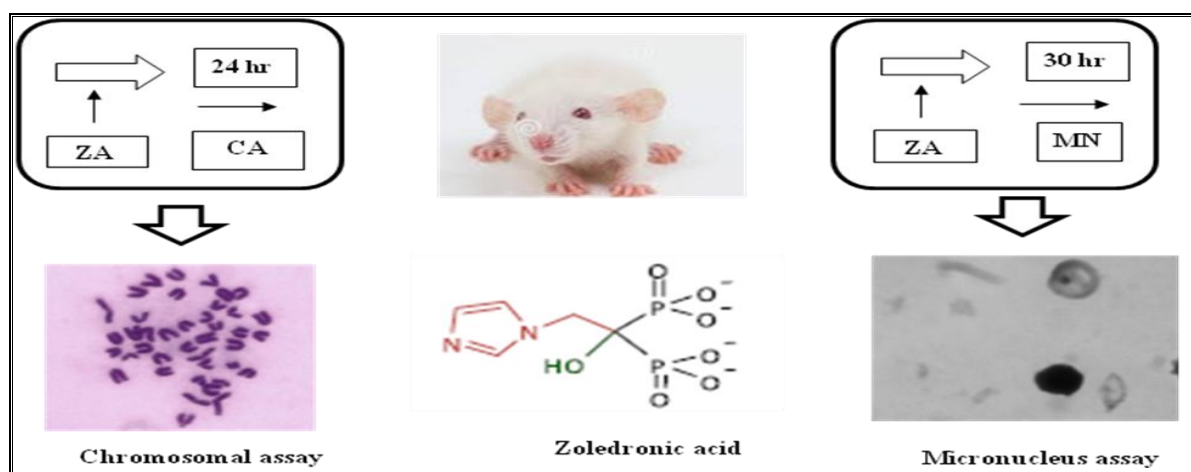
1b Evaluation of cytogenetic toxicity of Zoledronic acid on MDCK, VERO and NRK49-F cells (renal toxicity).

In vitro cytotoxicity was assessed by MTT assay done to evaluate cell inhibition. ZA induced a distinct dose dependent reduction of cell viability with an IC₅₀ value of (7.37±0.41 µM) in vero, (41.59±2.44 µM) NRK-49F and (102.77±3.38 µM) in MDCK cells respectively. ZA induced a significant number of MN in these renal cells at their respective IC₅₀ after incubation for 24h. Further ZA induced a cell cycle arrest at G₀/G₁ phase and subsequently decreased proportion of cells in G₂/M phases in all the renal cells at the respective IC₅₀ values. In view of the above-mentioned cell-inhibitory effects, experiments were also performed to determine whether ZA induced apoptosis in these cell lines, the results reveal the increase in Bax and decrease in Bcl₂ expression that indicates apoptosis.



2 Evaluation of short term and long term *in vivo* cytogenetic toxicity by Zoledronic acid on bone marrow cells of Swiss mice.

The *in vivo* assay was performed to understand the genotoxic effect of ZA on somatic cells of bone marrow in Swiss mice. Standard battery of tests were employed which include Chromosomal aberration test (CAT), Mitotic index (MI) and Micronucleus assay (MN) from bone marrow cells of Swiss mice albino. The slide were prepared by flame drying method and scanned under microscope, percentage of aberrations both including and excluding gaps were calculated.



Scheme: 2 concept of genotoxicity in somatic cells of Swiss mice.

The genotoxic potential of ZA was assessed by using bone marrow cells chromosomal aberration test at 24 h post-treatment. The percentage of aberrations both including and excluding gaps were calculated from the chromosomal aberrations scored from metaphase spreads. Mitotic index (MI) that gives information of percentage of dividing cells was also scored from the same slide. Micronucleus assay (MN) assay was done at 30h time point from both the bone marrow and peripheral blood of mice. The overall representation of toxicity study of ZA *in vivo* is demonstrated in **Scheme 2**.

The percentage of aberrant metaphase (20.1 ± 1.69), (20.67 ± 1.66), percentage of aberrations both (23.31 ± 1.44), (25.2 ± 0.96) including and excluding gaps (18.20 ± 1.15), (19.68 ± 1.38) were found to be significant ($P < 0.01$) in male and female mice exposed to 8mg/kg b.w respectively when compared to the vehicle control. However, there was no observed change in the mitotic index among the treatment groups. There was a significant induction of MN in the bone marrow of the female mice group treated with 4 and 8mg/kg b.w of ZA ($P < 0.01$).

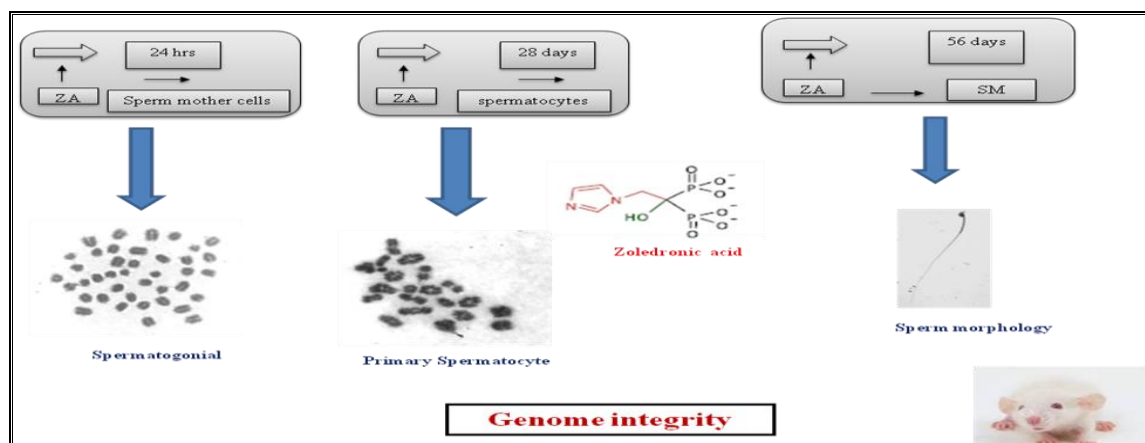


Scheme 3: Concept of genotoxicity in somatic cells of Swiss mice.

3 Evaluation of Cytogenetic toxicity profile long term: *in vivo* by Zoledronic acid on bone marrow cells of Swiss mice.

The long term genotoxic potential of ZA on bone marrow cells of mice was assessed by using chromosomal aberration test at week 4 post-treatment and week 8 was assessed for doses: 2, 4 and 8mg/kg/b.w respectively. The percentage of aberrant metaphase was found to be high (15.4 ± 0.71) which was found to be significant ($P < 0.001$). Percentage of aberrations both including (19.4 ± 2.37) and excluding gaps (9.05 ± 1.36) was found to be significant ($P < 0.01$) in female mice exposed to 8mg/kg b.w, when compared to the vehicle control. There were no observed changes in the mitotic index among the treated group of mice. However the incidence of MN in the mice was found to be significant ($P < 0.01$) in both the bone marrow (7.44 ± 1.51) and peripheral blood (6.71 ± 0.76). The overall representation was demonstrated in **Scheme 3**.

The percentage of aberrant metaphase (11.8 ± 0.29) and (11.9 ± 0.29) in male and female mice exposed to 4mg was found to be high which was found to be significant ($P < 0.001$). Percentage of aberrations both including (11.2 ± 0.41), (12.0 ± 0.08) and excluding gaps (7.75 ± 0.22), (8.31 ± 0.59) was found to be significant in male mice exposed to 8mg/kg b.w, when compared to the vehicle control ($P < 0.01$). There were no changes in the mitotic index among the treated group of mice. The incidence of MN in peripheral blood of mice was found to be significant (7.75 ± 0.08) in male group of mice ($P < 0.01$).



Scheme 4 concept of genotoxicity in germ cells of Swiss mice.

4 Assessment of toxicity profile of ZA on germline cells (Gonad: Testis) *in vivo* at; 24h, 4th week and 8th week post-treatment.

The genotoxic potential of ZA was assessed in germ cells of mice spermatogonial cell chromosomal aberration test at 24 h, primary spermatocytes at diakinesis stage were analyzed week 4 post-treatment and sperm morphology was assessed at week 8 post-treatment for doses: 2, 4 and 8 mg/kg/b.w of ZA respectively. Genotoxicity studies revealed a statistically significant higher number of abnormal spermatozoa (sperm) at week 8 post-treatment of both doses at 4 and 8 mg/kg of ZA (*Drug and chemical toxicology*, 2018, 1-7). Depicting the possible transmission of genotoxic effects from spermatogonial cells to sperm of male Swiss mice. Understanding of the mechanism underlying the genotoxicity in germline cells could possibly prevent genetic defects of the offspring among the cancer patients undergoing therapy. The overall consequences effecting genome integrity are demonstrated in **Scheme 4**.

Utility

Understanding the genotoxic effects on germline cells is very important, because effects of genotoxic agents can result in the interference with DNA replication machinery that in turn leads to change in the structural and numerical abnormalities at the chromosomal level, which are transmitted to the next generation. In addition, the factors enlisted above. Disruptions in spermatogenesis also depend on the epigenetic alterations during germ cell development. Cell division cycles which include mitosis and meiosis are vital for transmission of genetic material (chromosomes) from one generation to the next. As genome integrity is essential for survival and inheritance of traits to the offspring, similarly the genome stability is also vital for normal cell proliferation. It is of paramount importance to assess the genotoxicity induced by classical chemotherapeutic treatments in patients undergoing treatment. There is a higher chance of teratogenic effect associated with an increased risk in case of abnormal gonadal function. Ultimately leading to an anomalous reproductive outcome and genetic disease of the offspring. Aberrant chromosomal segregation is a consequence of errors in the series of programmed and sequential events occurring at prophase-I of meiosis defined by a number of characteristic morphological changes associated with the pairing of homologous chromosomes, synapsis, asynapsis and recombination. The spermatogonial cells upon subsequent cell divisions reach at spermatocyte-1 after week 4 (28 d) and chromosomes (bivalents) are observed at metaphase-1/diakinesis stage. This stage of chromosome provides valuable information about the induced aberrations at spermatogonial cells that have been transmitted to spermatocytes. The aberrations that could not be repaired in the spermatogonial cells subsequently appear as aberrant spermatocytes at metaphase-1/diakinesis stage, either with chromosomal deficiencies or with extra elements. This occurrence of univalents may be due to the asynapsis, i.e., failure in the pairing of homologous chromosomes, high percentage of aberrant spermatogonial cells, aberrant spermatocytes, and a higher number of abnormal sperms implicating the possible transmission of toxicity from spermatogonial cells to sperm level in mice. Abnormal sperm morphology is determined by several genes and due to their genetic damages; there is a possibility of causing the production of abnormal sperm morphology. If such defective sperm fertilizes with the normal ovum, there is a possibility of transmission of toxic effects to next generation.