Curriculum Vitae

Name: Shamsuddin Shaikh, Ph.D.

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Summary:

- 9 years of teaching experience at HCCS
- 15 years of research experience in chemistry and biochemistry
- Hands on experience in Organic and inorganic synthesis
- 5 years of experience in Protein Chemistry and enzyme kinetics
- 6 years of experience in Biochemical assays for Protein Tyrosine Kinase (PTK) inhibitors, and High Throughput Screening
- Hands on experience with integrated automated screening systems like Multiprobe Robotic Liquid Handling system, Tecan Polarian, TopCount Micro plate Scintillation and Luminescence counter
- 15 years of experience with analytical instruments: UV-Vis, FT-IR, HPLC, NMR (1H, ^{13}C, and hetero-nuclear), and Mass

Experience:

Chemistry Professor, August 2005 - Present
Houston Community College System
Houston, TX

Senior Scientist (May 2002- May 2005)
Signase, Inc.
Houston, TX

Faculty (Apr 1998 - Apr 2002)
Dept. of Neuro-Oncology,
University of Texas M.D. Anderson Cancer Center,
Houston, TX

Postdoctoral Fellow (Sept 1992 – Mar 1998)
Dept. of Clinical Investigations,
University of Texas M.D. Anderson Cancer Center,
Houston, TX

Education:

Ph.D. In Chemistry (1986-1992)
Osmania University, Hyderabad, India
Dissertation on "The Interaction of platinum and palladium dipeptide complexes with Nucleic acid constituents"

M.S. in Chemistry (1984-1986)
Osmania University, Hyderabad, India

B.S. in Chemistry and Biology (1981-1983)
Osmania University, Hyderabad, India

Certifications

- Safety in the Research and Clinical Laboratory Environment
- Safe Handling of Radioactive Materials in Research and Clinical laboratories

Under graduate research at Houston Community College (2009-present):

Selected students have been getting unique research experience in STEM areas supported by US Dept. of Education Grant in collaboration with University of St. Thomas since 2009.Various projects related to anti-cancer research have been carried out at HCC central. Our chemistry lab is very well equipped with FT-IR, Uv-Vis, GC-MS, HPLC and NMR.

Research Summary

I. Postdoctoral Fellow, UT M.D. Anderson Cancer Center, Houston, TX

Novel Cisplatin analogs as antitumor agents

Cisplatin is widely used to treat various types of human cancer. However, its spectrum of anti tumor activity is narrow and undesirable side effects and drug resistance limited its use in the clinic. Therefore new platinum drugs with equal or greater antitumor activity but less severe toxicities were sought.

I synthesized, and characterized novel platinum(II) and (IV) antitumor agents with *RR*, *SS*, and *Cis*-1, 2-diaminocyclohexane, *cis*-1, 4-diaminocyclohexane, cyclic, acyclic, and heterocyclic amines as non-leaving amine ligands. The complexes were characterized by elemental analysis, IR, UV-Vis, ^{1}H, ^{13}C, and ^{195}Pt NMR spectroscopy, HPLC, and X-ray crystallography. The complexes were tested *in vitro* and *in vivo* against L1210/0 (cisplatin sensitive), L1210/DDP (cisplatin resistant), and L1210/DACH (tetraplatin resistant) cell lines for their antitumor activity. Some of the complexes showed superior activity than cisplatin

II. Faculty, UT M.D. Anderson Cancer Center, Houston, TX

I worked on multiple projects related to protein tyrosine kinases (PTKs) and their inhibitors.

1. Investigation on the role of 2nd metal ion in PTKs

PTKs catalyze a bisubstrate phosphoryl-transfer reaction, with ATP-Mg complex as the phosphate donating substrate and a tyrosyl hydroxyl group in an appropriate protein structure as the phosphate acceptor. Mg^{2+} plays two essential roles in the catalytic activity of PTKs. It binds to ATP to form the phosphate-donating substrate, ATP-Mg complex (M1) and it also acts as an essential activator (M2). The role and mechanism of M1 in PTKs are fairly well studied and understood but there is little information concerning the role of M2 in PTKs.

I followed biophysical approach to investigate the role of M2 in PTK (CSK). A K_d of 2.6 mM and Quadrupolar coupling constant (χ_B) of 0.67 MHz for Mg^{2+} at M2 site was estimated by titrating CSK-GST with Mg^{2+} using ^{25}Mg NMR spectroscopy, while M1 was saturated with Cr^{3+}ATP. A distance between Cr^{2+} and Mn^{2+} at M1 and M2 sites respectively was calculated as 7.5 Å by measuring the effect of the paramagnetic Cr^{3+} ATP on the enzyme-bound Mn^{2+} using nuclear relaxation rate measurements.

These finding demonstrate that Mg^{2+} at M2 site in CSK retain the hydration shell and interact with enzyme through hydrogen bonding, and support the view that it activates CSK without effecting K_m for ATP-Mg.

2. Synthesis of β-methyl tyrosine and analogs

Synthesized rare amino acids, such as β-methyl tyrosine and analogs in the process of optimization of peptidomimetics as Protein Tyrosine Kinase (PTK) inhibitors

3. Lead identification.

In an afford to develop small molecule PTK inhibitors, I screened diversified libraries of organic small molecules against Src, CSK, and FGFr and identified hits using integrated automated screening platforms such as Packard Multiprobe Robotic Liquid Handling system, Tecan Polarian, TopCount Micro plate Scintillation and Luminescence counter. Determined the IC_{50} of hit compounds and studied the mechanism of inhibition.

III. Senior Scientist, Signase, Inc., Houston, TX

Signase, Inc. was a small biotech company started by our group and funded by Venture capitalists. The aim of the company was to develop small molecule inhibitors of protein tyrosine kinases.

As a Senior Scientist, I worked on different projects leading to the development of small molecule PTK inhibitors

1. Metal mediated PTK inhibitors

In the past quarter of a century many PTK inhibitors have been discovered and their mechanism of inhibition is competitive against the ATP substrate. In PTKs, such as the Src and Csk families, the second metal ion binds freely to the apoenzyme and does not affect the K_m for ATP-Mg and

is essential for catalysis. Physiologically, the second metal ion is also magnesium. Substitution studies have demonstrated that this magnesium ion can be replaced with higher affinity (10,000-fold) metals such as cobalt or zinc. Thus I hypothesized that stable metal chelate complexes could be prepared that would bind at the second metal ion site and inhibit PTK activity. I achieved a proof of concept by synthesizing a stable cobalt-L-tyrosinehydroxamate complex (IC_{50} = 1μM against Src). In contrast, free metal, tyrosine or the tyrosine hydroxamate were not inhibitory at 1 mM. This indicates a requirement for both the tyrosine hydroxamate moiety and for the metal moiety.

Several amino acid hydroxamates, amides, and Schiff base derivatives and their Cobalt complexes were synthesized and screened against Src, CSK, and FGFr.

2. High throughput screening.

Performed screening of small molecules against (PTKs), using integrated automated screening platforms such as Packard Multiprobe Robotic Liquid Handling system, Tecan Polarian, TopCount Micro plate Scintillation and Luminescence counter, calculated IC_{50}s, and determined the mechanism of enzyme inhibition

Publications

a. *Published and accepted articles in refereed journals:*

1. Synthesis, characterization, and X-ray crystal structures of cis-1,4-diaminocyclohexane-platinum(II) nucleobase adducts
   S.SHAMSUDDIN, MOHAMMAD S. ALI, KENTAN H. WHIMIRE and ABDUL R. KHOKHAR
   Poluhedron, 2007, 26, 637

2. Synthesis and characterization of novel trans mixed diamine platinum(II) and platinum(IV) complexes
   S.SHAMSUDDIN, MOHAMMAD S. ALI, S. HUANG, and ABDUL R. KHOKHAR
   J. Coor. Chem., 2002, 55, 659.

3. Synthesis, characterization and antitumor activity of new platinum(IV) axial carboxylate complexes: Crystal structure of potential antitumor agent [Pt^{IV}(*trans*-1*R*,2*R*-diamino-cyclohexane)*trans*(acetate)$_2$$Cl_2$]
   S. ROUNAQ ALI KHAN, S. SHAMSUDDIN, SHURONG HUANG, SADAAKI INUTSUKA, KENTAN H. WHITMIRE, ZAHID H. SIDDIK, AND ABDUL R. KHKHAR
   Bioorg. Med. Chem. Let., 2000, 8, 1.

4. Synthesis and characterization of a series of lipophilic cisplatin analogs with cis-1,4-diaminocyclohexane as non-leaving amine ligand
   S. SHAMSUDDIN, MOHAMMAD S. ALI, and A. R. KHOKHAR
   J. Coord. Chem., 1999, 40, 1.

5. Synthesis, characterization, and antitumor activity of new platinum(IV) *trans*-carboxylate complexes: Crystal structure of [Pt(*cis*-1,4-DACH)*trans*-(acetate)$_2$Cl$_2$].
S. SHAMSUDDIN, C. S. SANTILLAN, J. L. STARK, K. H. WHITMIRE, and A. R. KHOKHAR
J. Inorg. Biochem., 1998, 71, 29.

6. Synthesis and characterization of novel axial-dichloroplatinum(IV) cisplatin analogs:Crystal structure of an axial-dichloro complex [Pt(*cis*-1,4-DACH)*trans*-Cl$_2$(CBDCA)].1/2 MeOH.
S. SHAMSUDDIN, J. W. VAN HAL, J. L. STARK, K. H. WHITMIRE, and A. R. KHOKHAR
Inorg. Chem., 1997, 36, 5969.

8. Chemical and biological studies on a series of novel *(trans*-R,R)-, (*trans*-S,S)- and*cis*-1,2-diaminocyclohexaneplatinum(IV) carboxylate complexes.
A. R. KHOKHAR, S. SHAMSUDDIN, S. AL-BAKER, and Z. H. SIDDIK
J. Med. Chem., 1997, 40, 112.

9. Synthesis, characterization and antitumor activity of a series of novel cisplatin analogs with *cis*-1,4-diaminocyclohexane as a non-leaving amine group
S. SHAMSUDDIN, I.TAKAHASHI, Z.H. SIDDIK AND A. R. KHOKHAR
J. Inorg. Biochem., 1996, 61, 291.

10. Synthesis and antitumor activity of new *trans*-1R, 2R-diaminocyclohexane-platinum(II) complexes containing disubstituted sulfide group.
S.SHAMSUDDIN, S. AL-BAKER, Z. H. SIDDIK and A. R. KHOKHAR
Inorg. Chim. Acta, 1996, 241, 101.

11. Synthesis and characterization of new ethylenediamine and 1,1-bis(aminomethyl)cyclohexaneplatinum(II) complexes containing disubstituted sulfide as a leaving group.
S. SHAMSUDDIN, S. AL-BAKER, CHIRAYU SHAH and A. R. KHOKHA
J. Coord. Chem., 1995, 36, 7.

12. Mixed ligand complexes of platinum(II) and palladium(II) with glycyl-dl-methionine and nucleic acid constituents
BADAR TAQUI KHAN, S. SHAMSUDDIN and K. ANNAPOORNA
J. Coord. Chem., 1995, 36, 81.

13. Synthesis and crystal structure of a new antitumor agent:[Pt(*cis*-1,4-diaminocyclohexane)(1,1-cyclobutanedicarboxylate)]
S. SHAMSUDDIN and ABDUL R. KHOKHAR
J. Coord. Chem., 1994, 33, 83.

14. Synthesis and X-ray crystal structure of *cis*-1,4-diaminocyclohexanetetrachloro-platinum(IV): A new antitumor agent.
A. R. KHOKHAR, S. SHAMSUDDIN, and Q. XU
Inorg. Chim. Acta, 1994, 219, 193.

15. Mixed ligand complexes of cis-dichloromethioninepalladium(II) and *cis*-dichloro-ethioninepalatinum(II) with substituted pyrimidines.
BADAR TAQUI KHAN, S. SHAMSUDDIN, and K. ANNAPOORNA
Polyhedron, 1992, 11(16), 2109.

16. Crystal and molecular structure of chloroglycyl-*DL*-methioninatopalladium(II) monohydrate and its interaction with guanosine, cytosine and inosine.
BADAR TAQUI KHAN, S. SHAMSUDDIN and K. VENKATASUBRAMANIAN.
Polyhedron, 1992, 11(6), 671.

17. Synthesis, antimicrobial and antitumor activity of a series of palladium(II) mixed ligand complexes.
BADAR TAQUI KHAN, JAYASHREE BHATT, S. SHAMSUDDIN,
K.NAJMUDDIN and K. ANNAPOORNA.
J. Inorg. Biochem., 1991, 44(I), 53.

18. Crystal and molecular structure of *cis*-dichloroethioninepalatinum(II) and its interaction with adenine, hypoxanthine, cytosine and their nucleosides.
BADAR TAQUI KHAN, K. VENKATASUBRAMANIAN, S. SHAMSUDDIN,
K.NAJMUDDIN and S.M. ZAKEERUDDIN
Inorg. Chim. Acta, 1991, 179(1), 117.

19. Mixed ligand complexes of *cis*-dichloroethioninepalladium(II) with purines, pyrimidines and nucleosides.
BADAR TAQUI KHAN, S. SHAMSUDDIN, K. NAJMUDDIN and
S.M. ZAKEERUDDIN
Inorg. Chim. Acta, 1990, 170, 129.

b. *Manuscripts in preparation (preprints available)*

1. NMR studies on the role of 2nd metal ion in protein tyrosine kinase, csk
S. SHAMSUDDIN and RAYMOND J. A. BUDDE
In preparation for ***Biochemistry***

2. Cobalt(II) complexes as protein tyrosine kinase inhibitors
S. SHAMSUDDIN and RAYMOND J. A. BUDDE
In preparation for ***J. Med. Chem.***

4. Synthesis and Biological properties of novel *trans*-mixed amine platinum(II) and (IV)complexes.
S. SHAMSUDDIN**,** M. S, ALI, S. HUANG, Z. H. SIDDIK, and A. R. KHOLHAR
In preparation for ***J. Med. Chem.***

Presentations

1. Novel platinum(IV) cisplatin analogs as antitumor agents. R KHOKHAR, S. SHAMSUDDIN**,** and Z. H. SIDDIK, 89th Annual Meeting of the American Association for Cancer Research, New Orleans, March 28-April 1, **1998**

2. Synthesis and characterization of novel platinum(IV) cisplatin analogs S. SHAMSUDDIN, J. W. VAN HAL, J. L. STARK, K. H. WHITMIR, and A. R. KHOKHAR, 52nd ACS Southwest Regional Meeting, Houston, October 17-19, **1996.**

3. Chemical and biochemical pharmacological studies with novel platinum complexes. A. R. KHOKHAR, S. SHAMSUDDIN**,** I. TAKAHASHI, and Z. H. SIDDIK, 87th Annual Meeting of the American Association for Cancer Research, Washington D.C., April 20-24, **1996.**

4. Antitumor evaluation of novel platinum drugs in platinum resistance. A. R. KHOKHAR, S. SHAMSUDDIN, I. TAKAHASHI, and Z. H. SIDDIK, 86th Annual Meeting of the American Association for Cancer Research; Toronto, Ontario, Canada, March 18-22, **1995**.

5. Novel platinum drugs for circumventing platinum resistance. A. R. KHOKHAR, S. SHAMSUDDIN, I. TAKAHASHI, and Z. H. SIDDIK, 7th International Symposium on Platinum and other metal Coordination Compounds in Cancer Chemotherapy; Amsterdam, The Netherlands, March, 1-4, **1995**.

6. Novel platinum antitumor agents with *cis*-1, 4-diaminocyclohexane as non-leaving amine group. S. SHAMSUDDIN, I. TAKAHASHI, Z. H. SIDDIK, and A. R. KHOKHAR, XVI International Cancer Congress; New Delhi, India, Oct. 30-Nov. 5, **1994**.

6. Synthesis and antitumor activity of novel cisplatin analogs. A. R. KHOKHAR, S. SHAMSUDDIN, I. TAKAHASHI, and Z. H. SIDDIK, 30th International Conference on Coordination Chemistry, Kyoto, Japan, July 24-29, **1994**.

7. Chemical and biological studies of novel cisplatin analogs. A. R. KHOKHAR, S. SHAMSUDDIN, I. TAKAHASHI, and Z. H. SIDDIK, 85th Annual Meeting of the American Association for Cancer Research San Francisco, April 10-13, **1994**.

9. Interaction of chloglycy-*dl*-methioninatoplatinum(II) with purines, pyrimidines and nucleosides. S. SHAMSUDDIN, and B. T. KHAN, 204th American Chemical Society National Meeting; Washington D.C, August 23-28, **1992.**

10. Spectral and crystallographic studies of platinum(II) complexes with peptides and nucleic acid constituents. S. SHAMSUDDIN, K. ANNAPOORNA, and B. T. KHAN, 4th International Symposium on Modern Trends in Inorganic Chemistry; Bhavnagar, India, October 21-23, **1991**.