

MUHAMMAD SAEED, PhD

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CURRENT POSITION

Postdoctoral Scholar/Visiting Assistant Professor (2009-present)

Department of Chemistry, University of Iowa, Iowa City 52242

EDUCATION

Ph.D. Organic Chemistry (2001)

Department of Physical Biochemistry, Faculty of Chemistry and Pharmacy, University of Tübingen, Germany

Advisor: Prof. Wolfgang Voelter

Thesis Title: Asymmetric total syntheses of R-(-) argentilactone, S-(+)-argentilactone, R-(-)-massoilactone,(5S,6R)-O-acetylosmundalactone and series of as-triazines, trithiocarobate- and 4-piperazinyl derivatives on sugar templates.

M. Sc. Chemistry (1996)

University of the Punjab, Lahore

B.Sc. (Major Chemistry, Minor: Mathematics, Physics) (1994)

University of the Punjab, Lahore

PROFESIONAL EXPERIENCE

- **Postdoctoral Scholar**, University of Iowa, Iowa City, IA (2009-present)
- **Research Associate**, University of Nebraska Medical Center, Omaha, NE (2005-09)
- **Postdoctoral Research Associate**, University of Nebraska Medical Center, Omaha, NE (2001-04)
- **Research Officer**, HEJ Research Institute of Chemistry, University of Karachi, Karachi (1995-98)

RESEARCH EXPERIENCE AND ACHIEVEMENTS

Organic Syntheses

- Radiosyntheses of [¹¹C]N⁵,N¹⁰-methylenetetrahydrofolate and [¹⁴C]N⁵,N¹⁰-methylenetetrahydrofolate
- Accomplished large scale syntheses of catechol metabolites of natural and synthetic estrogens
- Synthesized hapten (small-molecules based immunogens) to generate antibody against depurinating adducts
- Asymmetric total syntheses of several natural products
- Accomplished chiral syntheses of several classes of pharmaceutically interesting compounds on carbohydrate templates (the Chiron Approach)

Chemical Carcinogenesis

- Investigated the formation of depurinating adducts in human cell lines
- Identified and quantified depurinating adducts in human urine
- Investigated the mechanism of cancer initiation by diethylstilbestrol (DES), benzene, and naphthalene
- Investigated mechanism of neurodegeneration by dopamine

Molecular Biology/Biochemistry

- DNA methylation profiling by bisulfite-based sequencing of promoter of estrogen receptor (ESR), progesterone receptor (PGR), aryl hydrocarbon receptor (AhR)
- Uptake of radiolabeled folates by human cancer cells lines
- Development of monoclonal antibodies against small organic molecules/development of hybridoma cultures
- Analyses of folate receptors, thymidylate synthase, estrogen receptor, progesterone receptor at transcription as well as at protein level by real-time PCR and western blots, respectively

TEACHING EXPERIENCE

Visiting Assistant Professor (2012)

Department of Chemistry, University of Iowa, Iowa City 52242

Principles of Chemistry 1 (Fall 2012 Chem004:011)

Visiting Assistant Professor (2011)

Department of Chemistry, University of Iowa, Iowa City 52242

Principles of Chemistry 1 (Fall 2011 Chem004:011)

Adjunct Chemistry Instructor (2010)

Muscatine Community College, Muscatine, Iowa, USA

General Chemistry (Spring 2010)

WORKSHOPS/COURSES

- Training Workshop for tumor biology and genomic implication in cancer-biology, University of Nebraska Medical Center, Omaha, NE USA.
- Breast Cancer research training at Eppley Cancer Institute, University of Nebraska Medical Center, Omaha, NE USA.
- Training workshop for mass-spectrometry (MS) and nuclear magnetic resonance (NMR) in structural biology, Eppley Cancer Institute, University of Nebraska Medical Center, Omaha, NE USA

AWARDS/HONORS

- Wagner Travel award for oral presentation in Gordon Isotope Conference in Galveston TX 2012
- Participated in the 50th annual meeting of Noble Laureates in Lindau, Germany 2000
- Deutscher Akademischer Austausch Dienst (DAAD) fellowship 1998-2001
- First Class First position 1996
- Gold medal/Role of Honor from the University of the Punjab, Lahore 1996

GRANT SUPPORT

- **ICTS Pilot grant:** University of Iowa \$50,000.00 Co-Principal Investigator
Effect of estrogen metabolism on S-adenosyl-L-homocysteine (SAM) homeostasis and ensuing DNA methylation changes at ER- α , PR, and RAR- β promoters. 2011-2012
- **EHSRC Pilot grant:** University of Iowa \$30,000.00 Principal Investigator
Development of Urinary Biomarkers of Herbicide Exposure and Susceptibility in an Exposed Rural Population 2011-2012

OUTREACH/COMMUNITY SERVICES

- 2009-present: Guiding graduate and undergraduate students in Amnon's Group
- 2011-present: Safety officer to implement regulations to reduce exposure to blood-borne pathogen
- 2011-present: Member of the judging panel for Eastern Iowa Science and Engineering Fair
- 2011-present: Reviewer for International Journals
- 2011-present: Grant/proposal reviewer for executive council of graduate and professional students, University of Iowa

PUBLICATIONS

1. Saeed, M.; Tewson, TJ.; Erdahl, CE.; Kohen, A., A fast chemoenzymatic synthesis of [11C]-N5,N10-methylenetetrahydrofolate as a potential PET tracer for proliferating cells. Nuc. Med. Biol. **2012**, 39, 697-701.

2. Cavalieri, E.; Saeed, M.; Zahid, M.; Cassada, D.; Snow, D.; Milkovic, M.; Rogan, E., Mechanism of DNA depurination by carcinogens in relation to cancer initiation. *IUMB Life* **2012**, 64, 169-79.
3. Kamel, M.; Shouman, S.; El-Merzebany, M.; Kilic, G.; Veenstra, T.; Saeed, M.; Wagih, M.; Diaz-Arrastia, C.; Patel, D.; Salama, S., Effect of tumour necrosis factor-alpha on estrogen metabolic pathways in breast cancer cells. *J. cancer* **2012**, 3, 310-21.
4. Zahid, M.; Saeed, M.; Yang, L.; Beseler, C.; Rogan, E.; Cavalieri, E., Formation of dopamine quinone-DNA adducts and their potential role in the etiology of Parkinson's disease. *IUBMB Life* **2011**, 63, (12), 1087-93.
5. Hinrichs, B.; Zahid, M.; Saeed, M.; Ali, M. F.; Cavalieri, E. L.; Rogan, E. G., Formation of diethylstilbestrol-DNA adducts in human breast epithelial cells and inhibition by resveratrol. *J Steroid Biochem Mol Biol* **2011**, 127, (3-5), 276-81.
6. Saeed, M.; Sheff, D.; Kohen, A., A novel positron emission tomography tracer distinguishes normal from cancerous cells. *J Biol Chem* **2011**, 286, (39), 33872-8.
7. Williams-Brown, M. Y.; Salih, S. M.; Xu, X.; Veenstra, T. D.; Saeed, M.; Theiler, S. K.; Diaz-Arrastia, C. R.; Salama, S. A., The effect of tamoxifen and raloxifene on estrogen metabolism and endometrial cancer risk. *J Steroid Biochem Mol Biol* **2011**, 126, (3-5), 78-86.
8. Zahid, M.; Saeed, M.; Beseler, C.; Rogan, E. G.; Cavalieri, E. L., Resveratrol and N-acetylcysteine block the cancer-initiating step in MCF-10F cells. *Free Radic Biol Med* **2011**, 50, (1), 78-85.
9. Zahid, M.; Saeed, M.; Ali, M. F.; Rogan, E. G.; Cavalieri, E. L., N-acetylcysteine blocks formation of cancer-initiating estrogen-DNA adducts in cells. *Free Radic Biol Med* **2010**, 49, (3), 392-400.
10. Zahid, M.; Saeed, M.; Rogan, E. G.; Cavalieri, E. L., Benzene and dopamine catechol quinones could initiate cancer or neurogenic disease. *Free Radic Biol Med* **2010**, 48, (2), 318-24.
11. Zahid, M.; Saeed, M.; Rogan, E. G.; Cavalieri, E. L., Benzene and dopamine catechol quinones could initiate cancer or neurogenic disease. *Free Radic Biol Med* **2009**.
12. Singh, S.; Zahid, M.; Saeed, M.; Gaikwad, N. W.; Meza, J. L.; Cavalieri, E. L.; Rogan, E. G.; Chakravarti, D., NAD(P)H:quinone oxidoreductase 1 Arg139Trp and Pro187Ser polymorphisms imbalance estrogen metabolism towards DNA adduct formation in human mammary epithelial cells. *J Steroid Biochem Mol Biol* **2009**, 117, (1-3), 56-66.
13. Salama, S. A.; Kamel, M. W.; Botting, S.; Salih, S. M.; Borahay, M. A.; Hamed, A. A.; Kilic, G. S.; Saeed, M.; Williams, M. Y.; Diaz-Arrastia, C. R., Catechol-o-methyltransferase expression and 2-methoxyestradiol affect microtubule dynamics and modify steroid receptor signaling in leiomyoma cells. *PLoS One* **2009**, 4, (10), e7356.
14. Saeed, M.; Rogan, E.; Cavalieri, E., Mechanism of metabolic activation and DNA adduct formation by the human carcinogen diethylstilbestrol: the defining link to natural estrogens. *Int J Cancer* **2009**, 124, (6), 1276-84.
15. Saeed, M.; Higginbotham, S.; Gaikwad, N.; Chakravarti, D.; Rogan, E.; Cavalieri, E., Depurinating naphthalene-DNA adducts in mouse skin related to cancer initiation. *Free Radic Biol Med* **2009**, 47, (7), 1075-81.
16. Zahid, M.; Gaikwad, N. W.; Ali, M. F.; Lu, F.; Saeed, M.; Yang, L.; Rogan, E. G.; Cavalieri, E. L., Prevention of estrogen-DNA adduct formation in MCF-10F cells by resveratrol. *Free Radic Biol Med* **2008**, 45, (2), 136-45.
17. Lu, F.; Zahid, M.; Wang, C.; Saeed, M.; Cavalieri, E. L.; Rogan, E. G., Resveratrol prevents estrogen-DNA adduct formation and neoplastic transformation in MCF-10F cells. *Cancer Prev Res (Phila Pa)* **2008**, 1, (2), 135-45.
18. Zahid, M.; Saeed, M.; Lu, F.; Gaikwad, N.; Rogan, E.; Cavalieri, E., Inhibition of catechol-O-methyltransferase increases estrogen-DNA adduct formation. *Free Radic Biol Med* **2007**, 43, (11), 1534-40.
19. Saeed, M.; Rogan, E.; Fernandez, S. V.; Sheriff, F.; Russo, J.; Cavalieri, E., Formation of depurinating N3Adenine and N7Guanine adducts by MCF-10F cells cultured in the presence of 4-hydroxyestradiol. *Int J Cancer* **2007**, 120, (8), 1821-4.
20. Saeed, M.; Higginbotham, S.; Rogan, E.; Cavalieri, E., Formation of depurinating N3adenine and N7guanine adducts after reaction of 1,2-naphthoquinone or enzyme-activated 1,2-dihydroxynaphthalene with DNA. Implications for the mechanism of tumor initiation by naphthalene. *Chem Biol Interact* **2007**, 165, (3), 175-88.

21. Lu, F.; Zahid, M.; Saeed, M.; Cavalieri, E. L.; Rogan, E. G., Estrogen metabolism and formation of estrogen-DNA adducts in estradiol-treated MCF-10F cells. The effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin induction and catechol-O-methyltransferase inhibition. *J Steroid Biochem Mol Biol* **2007**, 105, (1-5), 150-8.
22. Zahid, M.; Kohli, E.; Saeed, M.; Rogan, E.; Cavalieri, E., The greater reactivity of estradiol-3,4-quinone vs estradiol-2,3-quinone with DNA in the formation of depurinating adducts: implications for tumor-initiating activity. *Chem Res Toxicol* **2006**, 19, (1), 164-72.
23. Saeed, M.; Zahid, M.; Rogan, E.; Cavalieri, E., Synthesis of the catechols of natural and synthetic estrogens by using 2-iodoxybenzoic acid (IBX) as the oxidizing agent. *Steroids* **2005**, 70, (3), 173-8.
24. Saeed, M.; Zahid, M.; Gunselman, S. J.; Rogan, E.; Cavalieri, E., Slow loss of deoxyribose from the N7deoxyguanosine adducts of estradiol-3,4-quinone and hexestrol-3',4'-quinone. Implications for mutagenic activity. *Steroids* **2005**, 70, (1), 29-35.
25. Saeed, M.; Gunselman, S. J.; Higginbotham, S.; Rogan, E.; Cavalieri, E., Formation of the depurinating N3adenine and N7guanine adducts by reaction of DNA with hexestrol-3',4'-quinone or enzyme-activated 3'-hydroxyhexestrol. Implications for a unifying mechanism of tumor initiation by natural and synthetic estrogens. *Steroids* **2005**, 70, (1), 37-45.
26. Markushin, Y.; Kapke, P.; Saeed, M.; Zhang, H.; Dawoud, A.; Rogan, E. G.; Cavalieri, E. L.; Jankowiak, R., Development of monoclonal antibodies to 4-hydroxyestrogen-2-N-acetylcysteine conjugates: immunoaffinity and spectroscopic studies. *Chem Res Toxicol* **2005**, 18, (10), 1520-7.
27. Saeed, M.; Rogan, E.; Cavalieri, E., Novel spiro-quinone formation from 3'-hydroxydiethylstilbestrol after oxidation with silver oxide. *Tetrahedron Letters* **2005**, 46, (26), 4449-4451.
28. Abdel-Jalil, R. J.; Voelter, W.; Saeed, M., A novel method for the synthesis of 4(3H)-quinazolinones. *Tetrahedron Letters* **2004**, 45, (17), 3475-3476.
29. Dolashka-Angelova, P.; Schwarz, H.; Dolashki, A.; Stevanovic, S.; Fecker, M.; Saeed, M.; Voelter, W., Oligomeric stability of Rapana venosa hemocyanin (RvH) and its structural subunits. *Biochim Biophys Acta* **2003**, 1646, (1-2), 77-85.
30. Saeed, M.; Abbas, M.; Abdel-Jalil, R. J.; Zahid, M.; Voelter, W., A convenient method for the synthesis of cyclic trithiocarbonates on carbohydrate scaffolds. *Tetrahedron Letters* **2003**, 44, (2), 315-317.
31. Saeed, M.; Abbas, M.; Heinrich, A.; Voelter, W., An efficient approach to the synthesis of tri-substituted iminothiazolidenes and their effects on the human neuroblastoma cell line. *Tetrahedron Letters* **2003**, 44, (32), 6107-6110.
32. Zahid, M.; Saeed, M.; Asim, M.; Ishrud, O.; Wu, S. H.; Ahmad, V. U.; Pan, Y. J., New glycosides from Salvia moorcroftiana (Lamiaceae). *Helvetica Chimica Acta* **2003**, 86, (6), 2021-2027.
33. Khan, K. M.; Saify, Z. S.; Shah, S. T.; Ahmed, M.; Saeed, M.; Hayat, S.; Abbas, M.; Voelter, W., Syntheses, antibacterial, cytotoxic and antifungal effects of new 3-carboxy-1-phenacylpyridinium salts. *Arzneimittelforschung* **2002**, 52, (4), 286-93.
34. Cavalieri, E. L.; Li, K. M.; Balu, N.; Saeed, M.; Devanesan, P.; Higginbotham, S.; Zhao, J.; Gross, M. L.; Rogan, E. G., Catechol ortho-quinones: the electrophilic compounds that form depurinating DNA adducts and could initiate cancer and other diseases. *Carcinogenesis* **2002**, 23, (6), 1071-7.
35. Khan, K. M.; Saify, Z. S.; Shah, S. T. A.; Ahmed, M.; Saeed, M.; Hayat, S.; Abbas, M.; Voelter, W., Syntheses, antibacterial, cytotoxic and antifungal effects of new 3-carboxy-1-phenacylpyridinium salts. *Arzneimittel-Forschung-Drug Research* **2002**, 52, (4), 286-293.
36. Abdel-Jalil, R. J.; Saeed, M.; Voelter, W., An expeditious approach to tri-substituted chiral thiazolines. *Tetrahedron Letters* **2001**, 42, (13), 2435-2437.
37. Saeed, M.; Abbas, M.; Khan, K. M.; Voelter, W., Total synthesis of S-(+)-argentilactone. *Zeitschrift Fur Naturforschung Section B-a Journal of Chemical Sciences* **2001**, 56, (3), 325-328.
38. Saeed, M.; Abdel-Jalil, R. J.; Voelter, W.; El-Abadelah, M. M., An expeditious synthesis of optically pure 1,4,5,6-tetrahydro-as-triazines, fused to the carbohydrate skeleton. *Chemistry Letters* **2001**, (7), 660-661.
39. Saeed, M.; Ilg, T.; Schick, M.; Abbas, M.; Voelter, W., Total synthesis and anti-leishmanial activity of R-(+)-argentilactone. *Tetrahedron Letters* **2001**, 42, (42), 7401-7403.
40. Khan, K. M.; Saify, Z. S.; Khan, Z. A.; Ahmed, M.; Saeed, M.; Schick, M.; Kohlbau, H. J.; Voelter, W., Syntheses and cytotoxic, antimicrobial, antifungal and cardiovascular activity of new quinoline derivatives. *Arzneimittelforschung* **2000**, 50, (10), 915-24.

41. Abdel-Jalil, R. J.; Saeed, M.; Heeg, P.; Voelter, W., Synthesis and properties of selected 4-substituted anhydro sugars. *Zeitschrift Fur Naturforschung Section B-a Journal of Chemical Sciences* **2000**, 55, (7), 661-666.
42. Khan, K. M.; Saify, Z. S.; Zeeshan; Khan, A.; Ahmed, M.; Saeed, M.; Abdel-Jalil, R. J.; Grubler, G.; Voelter, W., Syntheses of selected quaternary phenacylbromopyridinium compounds and their biological evaluation. *Zeitschrift Fur Naturforschung Section B-a Journal of Chemical Sciences* **1999**, 54, (9), 1210-1218.
43. Saify, Z. S.; Khan, K. M.; Haider, S. M.; Zeeshan; Shah, S. T. A.; Saeed, M.; Shekhani, M. S.; Voelter, W., Syntheses and evaluation of the analgesic activity of some 4-acetyl-4-phenylpiperidine and 4-hydroxy-4-phenylpiperidine derivatives. *Zeitschrift Fur Naturforschung Section B-a Journal of Chemical Sciences* **1999**, 54, (10), 1327-1336.

ORAL PRESENTATIONS

1. ***Formation of estrogen-homocysteine conjugates in humans: A pilot study to investigate mechanism of S-adenosyl-L-methionine (SAM) depletion and initiation of diseases***, Institute of Clinical and Translational Science, University of Iowa, IA, April 2012.
2. ***Targeting thymidylate synthase activity and folate receptors to assess therapeutic response and cancer imaging by positron emission tomography (PET)***, Gordon Conference on isotopes in Chemical & Biological Science, Gelveston, TX, Feb 2012.