

Professor Richard B. van Breemen, University of Illinois, Chicago, USA



We interviewed Professor Richard B. van Breemen who is studying medicinal properties of natural products at the University of Illinois, College of Pharmacy, in Chicago, using advanced mass spectrometry. Recently he found that lycopene (the red carotenoid in tomatoes) could reduce risk of prostate cancer. Shimadzu has been supporting Prof. van Breemen's laboratory for six years, by providing Shimadzu's state-of-the-art mass spectrometry such as IT-TOF, LCMS-8040 and LCMS-8050.

Shimadzu:

First, could you outline your research and achievements?

Prof. van Breemen:

My research group investigates natural cancer chemoprevention agents and the safety and efficacy of botanical dietary supplements. We specialize in mass spectrometric studies of natural products that span the range from discovery to clinical investigation. An early proponent of MS-based screening, we use our ultrafiltration-mass spectrometry approach to find pharmacologically active compounds in complex natural product extracts. Then, we use high resolution LC-MS/MS to investigate the metabolism of lead compounds. Finally in support of clinical trials, we use quantitative UHPLC-MS-MS to measure levels of the active natural products and their metabolites as well as biomarkers of efficacy in clinical specimens.

Some of our most successful projects have included studies of carotenoid bioavailability and chemoprevention that are exemplified by our clinical trials of prostate cancer chemoprevention by the tomato carotenoid lycopene. As I am director of the oldest academic center in the United States focused on the safety and efficacy of botanical dietary supplements (UIC/NIH Center for Botanical Dietary Supplements Research), we help to safeguard women's health by investigating mechanisms of action and safety of botanicals used by menopausal women as alternatives to conventional estrogen replacement therapy. Qualitative and quantitative applications of mass spectrometry are essential at every stage of these botanical dietary supplement studies.

Shimadzu:

Why are you interested in those fields?

Prof. van Breemen:

Our interest in natural products as sources of new drugs is based on the fact that at least half of all existing pharmaceuticals are natural products or are derived from them, which should be no surprise as Nature has already preselected these substances for bioactivity. Now that most major pharmaceutical companies have abandoned their natural products drug discovery programs, our search for new natural pharmaceutical agents has become even more imperative. Since the Women's Health Initiative indicated that conventional estrogen replacement therapy might increase risks of certain forms of cancer, cardiovascular disease and even dementia, many women have sought relief from menopausal symptoms by using botanical dietary supplements with the expectation that they may be safer as well as effective. In response, our Botanical Center is working to ensure the safety of these botanical products as well to determine their mechanisms of action and potential efficacy.

Shimadzu:

Then, your article in this journal addresses the quantitative analysis of bisphenol A (BPA) in water using the LCMS-8050. Why are biomedical researchers concerned about human exposure to BPA?

Prof. van Breemen:

BPA is a high volume industrial product used in a wide range of consumer products from polycarbonate bottles to epoxy resins lining the inside of canned foods. The release of BPA into the environment might result in its accumulation in lakes and rivers where it might affect aquatic wildlife due to its endocrine disruption activity. There is particular concern that exposure of children to endocrine disrupting chemicals like BPA might be especially significant.

Shimadzu:

How are our instruments helping you?

Prof. van Breemen:

My research group has witnessed many innovations in mass spectrometry and chromatography over the last 25+ years that include the introduction of novel ionization techniques such as MALDI and electrospray, the invention of new tandem mass spectrometers such as MALDI TOF/TOF and IT TOF instruments, and the introduction of UHPLC. All of these innovations contribute to our research by enabling faster MS-based screening of botanical and marine extracts, faster structural characterization of natural product lead compounds and faster and more sensitive quantitative analysis in support of preclinical and clinical studies.

Shimadzu:

What are Shimadzu's strengths compared to other companies? (not limited to the instruments)

Prof. van Breemen:

For many years, Shimadzu has been a leader in HPLC and UHPLC by providing highly reliable as well as high performance chromatography instrumentation. Shimadzu is also highly respected for providing high quality service support. In the field of MALDI TOF/TOF, Shimadzu offers the highest performance and features not available from most vendors due to innovations such implementation of the late Prof. Robert Cotter's curved-field reflectron and high-energy CID features, which facilitate structural studies using charge-remote fragmentation. Shimadzu's high resolution IT-TOF mass spectrometer offers MSⁿ capabilities not obtainable with QqTOF instruments, and Shimadzu continues to lead the world in fast triple quadrupole mass spectrometer technology with the LCMS-8030, LCMS-8040 and now the fastest scanning and most sensitive of all, the LCMS-8050.

Shimadzu:

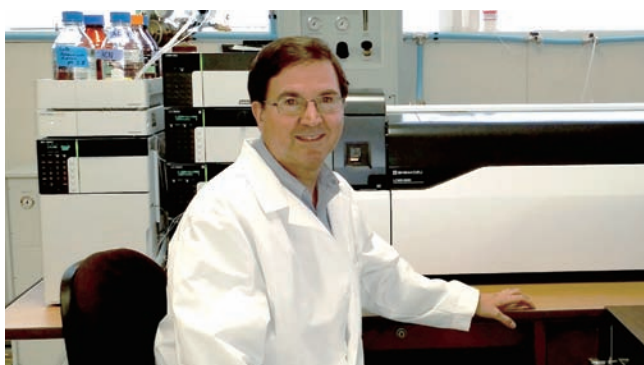
Finally, can you please share any requests that you have with respect to analytical instrument vendors?

Prof. van Breemen:

Like most academic biomedical mass spectrometry laboratories, we are always pushing the limits of technology in terms of speed and sensitivity in the analysis of clinical and research specimens. Fortunately, the performance specifications of mass spectrometers continue to increase and thereby enable us to be more productive than ever. For example, we are looking forward to seeing how much more research we can accomplish each day using Shimadzu's new LCMS-8050 triple quadrupole mass spectrometer.

Shimadzu:

Thank you very much.



Here are selected 2013 publications citing Shimadzu mass spectrometers (7 out of 15 for 2013):

And here are the latest publications by Prof. van Breemen :

- (1) Nikolic D, van Breemen RB. Analytical methods for quantitation of prenylated flavonoids from hops. *Curr. Anal. Chem.* 9, 71-85 (2013).
- (2) Yuan Y, Yu L-F, Qiu X, Kozikowski AP, van Breemen RB. Pharmacokinetics and brain penetration of LF-3-88, (2-[5-[5-(2(S)-azetidylmethoxy)-3-pyridyl]-3-isoxazolyl]-ethanol, a selective $\alpha 4 \beta 2$ -nAChR partial agonist and promising antidepressant. *J. Chromatogr. B* 912, 38-42 (2013).

- (3) Gaba RC, Yap FY, Martinez EM, Li Y, Guzman G, Parvinian A, van Breemen RB, Kumar N. Transarterial sorafenib chemoembolization: preliminary study of technical feasibility in a rabbit model. *J. Vasc. Interv. Radiol.* 24, 744-750 (2013).

- (4) Conda-Sheridan M, Park EJ, Beck DE, Reddy PV, Nguyen TX, Hu B, Chen L, White JJ, van Breemen RB, Pezzuto JM, Cushman M. Design, synthesis, and biological evaluation of indenoisoquinoline rexinoids with chemopreventive potential. *J. Med. Chem.* 56, 2581-2605 (2013).

- (5) Yu R, Zhao G, Christman JW, Xiao L, van Breemen RB. Method development and validation for ultra-high pressure liquid chromatography/tandem mass spectrometry determination of multiple prostanoids in biological samples. *J. AOAC Intl.* 96, 67-76 (2013).

- (6) Hajirahimkhan A, Simmler C, Yuan Y, Anderson JR, Chen SN, Nikolić D, Dietz BM, Pauli GF, van Breemen RB, Bolton JL. Evaluation of estrogenic activity of licorice species in comparison with hops used in botanicals for menopausal symptoms. *PLoS One* 8(7):e67947 Jul 12 (2013). doi: 10.1371/journal.pone.0067947

- (7) Andreani A, Leoni A, Locatelli A, Morigi R, Rambaldi M, Cervellati R, Greco E, Kondratyuk TP, Park E-J, Huang K, van Breemen RB, Pezzuto JM. Chemopreventive and antioxidant activity of 6-substituted imidazo[2,1-b]thiazoles. *Eur. J. Med. Chem.* 68C, 412-421 (2013).