Chromium Status and Health: Accurate and Precise Analysis Using High Resolution ICP-MS
by David W. Quig, PhD and Dean Bass, PhD

Abstract
Accurate and precise measurement of chromium (Cr) in biological specimens is critical for valid assessment of the status of this essential element. Appropriate Cr supplementation is clearly justified for all forms of diabetes, hyperinsulinemia and some types of hyperlipidemia. Presently, however, few laboratories can accurately measure true Cr concentrations primarily because of limitations associated with analytical instruments that are widely utilized. These limitations are a result of the low concentrations of Cr in biological specimens and interferences associated with low-level Cr measurements. A specialized type of inductively coupled plasma mass spectrometry (ICP-MS), High Resolution (HR) ICP-MS has been developed which permits accurate determination of Cr by clear separation of the element from interferences that have grossly similar, but precisely distinct, molecular mass. The purpose of this article is to briefly highlight the physiological role of Cr as it relates to preventive and natural medicine and, describe the basic principles and advantages of HR-ICP-MS.

Cr Homeostasis
Cr is an essential element that potentiates insulin action and thereby affects carbohydrate, lipid and protein metabolism. Oral absorption of Cr is relatively low, like other trivalent elements, and dependent upon the level of intake, the form of the element, mass competition by other elements present in the gastrointestinal tract, and the presence of other dietary substances such as oxalates and phytates. In addition to low oral bioavailability (< 2%), it is apparent from population studies that the majority of people in the US, Canada, the UK and Finland do not obtain the Estimated Safe and Adequate Daily Dietary Intake of 50-200 mg Cr/day. Refining grains and food processing removes the bulk of bioavailable Cr. Organic forms of Cr (eg. picolinate, nicotinate, histidate) are absorbed much more efficiently than inorganic Cr chloride, and Cr from whole foods and brewers yeast has by far the highest bioavailability. Elements that compete for Cr absorption include calcium, manganese, zinc and iron. Oxalates, ascorbic acid, and starch enhance Cr absorption. High intake of simple sugars, and hyperinsulinemia increase Cr excretion in the urine as much as 300%. Strenuous running also increases urinary excretion of Cr. Chronic use of corticosteroids or certain antacids also compromise Cr status, as does aging, infection and trauma.

Cr in Health and Disease
The primary physiological role of Cr is in its regulation of glucose homeostasis and insulin responsiveness. Chromium potentiates insulin activity in insulin responsive cells such as skeletal muscle, heart, liver, and adipose tissue. The putative role of Cr in the "glucose tolerance factor" (GTF) is unresolved but GTF appears to be the transporter of Cr to intracellular proteins. A lower molecular weight Cr binding oligopeptide appears responsible for the insulin potentiation or amplification in the cell once insulin has bound to the insulin receptor.

Numerous studies have documented the beneficial roles of Cr supplementation in diabetes, both types I and II, hypoglycemia, hyperglycemia/hyperinsulinemia, obesity, mixed hyperlipidemia and gestational diabetes. Due to its involvement in the regulation of blood glucose, insulin, triglycerides, and total

Table 1. Elements benefiting from HR-ICP-MS reducing interferences.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Mass</th>
<th>Interferant</th>
<th>Mass</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>31P</td>
<td>30.9738</td>
<td>NOH</td>
<td>31.0058</td>
<td>966</td>
</tr>
<tr>
<td>32S</td>
<td>31.9721</td>
<td>O2</td>
<td>31.9898</td>
<td>1800</td>
</tr>
<tr>
<td>39K</td>
<td>38.9637</td>
<td>Ar</td>
<td>38.9706</td>
<td>5688</td>
</tr>
<tr>
<td>51V</td>
<td>50.9440</td>
<td>ClO</td>
<td>50.9638</td>
<td>2572</td>
</tr>
<tr>
<td>52Cr</td>
<td>51.9405</td>
<td>ArC</td>
<td>51.9624</td>
<td>2364</td>
</tr>
<tr>
<td>56Fe</td>
<td>55.9349</td>
<td>ArO</td>
<td>55.9573</td>
<td>2502</td>
</tr>
<tr>
<td>75As</td>
<td>74.9216</td>
<td>ArCl</td>
<td>74.9323</td>
<td>7772</td>
</tr>
<tr>
<td>80Se</td>
<td>79.9165</td>
<td>Ar2</td>
<td>79.9248</td>
<td>9693</td>
</tr>
</tbody>
</table>

Figure 1. Conventional ICP mass spectrum
and low-density lipoprotein cholesterol levels, Cr status has obvious implications in the atherosclerotic process. Excellent reviews of the clinical use and metabolism of chromium have been published by Broadhurst\textsuperscript{2} and Lamson.\textsuperscript{30}

**Assessment of Cr Status**

Valid, direct assessment of Cr status has evaded scientists and practitioners for many years, primarily due to analytical problems. Once absorbed, Cr in blood is bound and transported to tissues in association with transferrin and to a lesser extent, albumen. Transfer of Cr from the serum/plasma compartment to tissues is rapid, and excretion occurs primarily in the urine with lesser amounts excreted in the bile, sweat and hair.\textsuperscript{31} Tissue Cr stores do not appear to be in equilibrium with serum Cr, thus a change in fasting serum or plasma Cr concentration is not a sensitive indicator of a mild change in Cr status.\textsuperscript{8} Further, serum and urine C levels can fluctuate considerably and therefore have not been accepted as reliable indicators of body Cr status.\textsuperscript{31} Tissue Cr levels are one-to-two orders of magnitude greater than blood Cr.\textsuperscript{9} Prior to the application of HR-ICP-MS, analytical determination of Cr in whole blood, red blood cells or white blood cells has been problematic. With the markedly greater sensitivity and accuracy offered by HR-ICP-MS, it is now possible to utilize whole blood or blood cell Cr levels to directly assess Cr status.

**High Resolution Inductively Coupled Plasma-Mass Spectrometry**

*How it works.* The ICP-MS works by aspirating a liquid sample into a high temperature argon ion plasma. In this plasma, ions are formed from the elements in the sample. The analyte (elements of clinical significance) ions are introduced to the mass spectrometer where they are identified, based upon their mass, and quantified, based upon a comparison of the intensity of each mass to known standards and controls. In regular ICP-MS, this mass spectrometer is a quadrupole and in HR-ICP-MS the mass spectrometer is an electrostatic field and a magnetic sector. For this reason, this type of mass spectrometer is often referred to as double focusing or magnetic sector. All quadrupole data presented in this paper are from a Perkin-Elmer Elan 6000 ICP-MS and all high-resolution data are from a ThermoElemental Axiom HR-ICP-MS.

**High Resolution, More Accurate.** The quadrupole ICP-MS is typically accurate for elements greater than mass 80. Because the quadrupole is only capable of distinguishing masses 1 unit apart (i.e., 51 from 52 or 208 from 209), molecular species may form which are interferences at specific masses. This occurs most often at masses 80 and below. HR-ICP-MS can distinguish between the analyte of interest and potential interferences. For example, it can distinguish between chromium (mass 51.9405) and molecules formed during the analysis of clinical samples, such as, argon-carbide (mass 51.9624). Table 1 shows typical elements that benefit from the HR-ICP-MS. Figures 1 and 2 show typical mass spectrums from conventional ICP-MS and HR-ICP-MS. Figure 1 shows the mass spectrum from standard quadrupole ICP-MS. In this case, both chromium and argon carbide exist at mass 52, and both iron and argon oxide exist at mass 56. Complicated corrections must be made. The HR-ICP-MS is capable of resolving these molecular peaks from the analytes of clinical significance (Figure 2). Because of the unambiguous identification of elements using HR-ICP-MS, it is often used as the standard in comparing and establishing known values for trace elements.

**High Resolution, More Sensitive (Lower Detection Limits).** Ion transmission in HR-ICP-MS is much higher than conventional ICP-MS. Ion transmission refers to the number of ions that make it through the mass spectrometer to the detector. For example, 100 mercury ions enter the mass spectrometer and 90 reach the detector. This larger percentage of ions reaching the detector in HR-ICP-MS results in greater sensitivity. In addition, HR-ICP-MS has lower background counts, resulting in more stable readings at low levels and

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ultimately, even lower detection limits. Typical detection limits for HR-ICP-MS is parts-per-trillion and sub-parts-per-trillion. This compares to sub-parts per billion and parts-per-trillion for conventional ICP-MS (10 to 100 times difference). Lower detection limits means more accurate and precise low level measurements for all elements. Table 2 shows typical instrument detection limits for HR-ICP-MS and conventional ICP-MS.

HR-ICP-MS has been around since the late 1980s and has been used by geological, semiconductor, nuclear industries, material sciences, environmental, chemical, and clinical industries. Most clinical work has been in research hospitals or government agencies (US Centers for Disease Control, CDC). It is also used at government standards setting agencies such as the National Institute of Standards and Technology (NIST).

Table 2

<table>
<thead>
<tr>
<th>Element</th>
<th>HR-ICP-MS DL (ppb)</th>
<th>ICP-MS DL (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mercury</td>
<td>0.004</td>
<td>0.2</td>
</tr>
<tr>
<td>Lead</td>
<td>0.006</td>
<td>0.06</td>
</tr>
<tr>
<td>Uranium</td>
<td>0.0009</td>
<td>0.01</td>
</tr>
<tr>
<td>Thallium</td>
<td>0.0008</td>
<td>0.1</td>
</tr>
<tr>
<td>Molybdenum</td>
<td>0.002</td>
<td>0.1</td>
</tr>
<tr>
<td>Chromium</td>
<td>0.004</td>
<td>0.1</td>
</tr>
<tr>
<td>Vanadium</td>
<td>0.001</td>
<td>0.07</td>
</tr>
<tr>
<td>Lithium</td>
<td>0.002</td>
<td>0.1</td>
</tr>
</tbody>
</table>

About the Authors

Dr. Quig is Vice-President, Scientific Support for Doctor’s Data, Inc. where he continues to design and implement research and laboratory tests pertaining to the dynamic interplay between nutrition, metabolism and environmental toxins. Dr. Quig also consults with physicians about test results and chelation protocols, and presents lectures related to metal toxicity and nutrition at national and international medical conferences on a regular basis. Dr. Quig received his Masters degree in Human Nutrition from Virginia Tech, Blacksburg, Virginia, in 1980 and his PhD in Nutritional Biochemistry from the University of Illinois, Champaign, IL, in 1984. For the subsequent 12 years he performed and published basic biomedical research as a Research Associate at Cornell University and as a Senior Research Pharmacologist at a major pharmaceutical company.

Dr. Bass is a Technical Supervisor for Doctor’s Data, Inc. where he is responsible for overseeing all quality assurance and control programs. Dr. Bass’ focus has been on research and operations in the areas of atomic spectroscopy, trace metal analysis and metal speciation. Dr. Bass earned his doctorate in analytical chemistry in 1988 from the University of Texas in Austin and gained expertise in chemical and scientific methodology as an analytical chemist and group leader at Argonne National Laboratory in Illinois and prior to that, as an applications scientist at Hitachi Instruments, Inc. in Danbury, Connecticut.

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References


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