Definition from an animal nutrition point of view

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BfR-Symposium
“The Role of Bioavailability in Risk Assessment using the Example of Trace Elements”
16.01.2013 - 17.01.2013
Agenda

• Potential prospects
• Definition
• Limitations
• Conclusions
Bioavailability in animal nutrition

• The term is generally used to describe properties of absorption and utilisation of nutrients including the optimal conversion from feed to performance, health and products.

• The term can be also used (indirectly) for estimations of environmental contamination.
Potential prospects of bioavailability in animal nutrition

- Comparison of mineral sources
- Efficacy of nutrients and additives
- Quality and safety of products
- Economical aspects
- Environmental contamination
- Animal health

Bioavailability
Definition of bioavailability

O`Dell 1983:

“Bioavailability in terms of minerals may be defined as the proportion of an ingested mineral that is absorbed, transported to its site of action, and converted to the physiological active species“

Ammermann et al. 1995:

“Degree to which an ingested mineral is absorbed in a form that can be utilized in metabolism by the normal animal“

Fuller 2004:

“Bioavailability is that proportion of a dietary nutrient that is absorbed and may then be utilized by an animal for physiological function(s)“
Evaluation of bioavailability in animal nutrition

- Digestible level
  - Absorptive level
    - Metabolic level
      - Specific criteria
        - Presence in fluid and tissues
  - Dietary level
  - Absorptive level
    - Metabolic level
      - Specific criteria
        - Presence in fluid and tissues
  - Dietary level
  - Absorptive level
    - Metabolic level
      - Specific criteria
        - Presence in fluid and tissues
Bioavailability in animal nutrition

• The term is generally used to describe properties of absorption and utilisation of nutrients including the optimal conversion from feed to performance, health and products

• The term is also used for estimations of environmental contamination and risk assessment

• Absorption and intermediary utilisation of minerals varies according to numerous factors
Specifics of bioavailability of trace minerals included in diets

- Supply
  - Trace mineral contents in ingredients + mineral composition of premixes
  - But trace mineral contents in ingredients are estimated to be zero
  ➔ Supplementation of trace minerals by using premix meeting the overall requirement + safety levels
Year of research used in estimate of trace mineral requirements (NRC, 1994, GfE, 1999/poultry; 2006/pigs)

<table>
<thead>
<tr>
<th>Source</th>
<th>Pigs</th>
<th>Broilers</th>
<th>Layers</th>
</tr>
</thead>
</table>

Dearth of research in trace mineral nutrition over the last 20 to 30 years
## NRC mineral levels for pigs and those recommended by industry

<table>
<thead>
<tr>
<th>Source</th>
<th>NRC 1998 mg/kg (88% DM)</th>
<th>Commercial additions mg/kg (88% DM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe</td>
<td>80</td>
<td>100 - 200</td>
</tr>
<tr>
<td>Mn</td>
<td>20</td>
<td>40 - 80</td>
</tr>
<tr>
<td>Zn</td>
<td>50</td>
<td>100 - 150</td>
</tr>
<tr>
<td>Cu</td>
<td>5</td>
<td>10 - 20</td>
</tr>
<tr>
<td>Se</td>
<td>0.15</td>
<td>0.2 - 0.5</td>
</tr>
<tr>
<td>I</td>
<td>0.14</td>
<td>0.15 - 0.50</td>
</tr>
</tbody>
</table>
NRC mineral levels for poultry and those recommended by industry

<table>
<thead>
<tr>
<th>Source</th>
<th>NRC 1994 mg/kg (88% DM)</th>
<th>Commercial additions mg/kg (88% DM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe</td>
<td>80</td>
<td>100 - 220</td>
</tr>
<tr>
<td>Mn</td>
<td>60</td>
<td>80 - 120</td>
</tr>
<tr>
<td>Zn</td>
<td>40</td>
<td>40- 150</td>
</tr>
<tr>
<td>Cu</td>
<td>8</td>
<td>10 - 20 (150)</td>
</tr>
<tr>
<td>Se</td>
<td>0.15</td>
<td>0.20 - 0.30</td>
</tr>
<tr>
<td>I</td>
<td>0.35</td>
<td>1 - 2</td>
</tr>
</tbody>
</table>
Ranges of trace mineral levels in typical diets for poultry meat production (mg/kg (88% DM))

<table>
<thead>
<tr>
<th></th>
<th>Fe</th>
<th>Mn</th>
<th>Zn</th>
<th>Cu</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contribution of native components</td>
<td>45 - 180</td>
<td>10 - 30</td>
<td>18 - 30</td>
<td>6 - 15</td>
<td>0.06 - 0.5</td>
</tr>
<tr>
<td>Requirement (NRC 1994)</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>8</td>
<td>0.35</td>
</tr>
<tr>
<td>Commercial additions</td>
<td>20 - 120</td>
<td>80 - 120</td>
<td>40 - 150</td>
<td>10 - 20 (150)</td>
<td>1 - 2</td>
</tr>
</tbody>
</table>
Specifics of bioavailability of trace minerals included in diets

• Supply
  - Trace mineral contents in ingredients + mineral composition of premixes
  - But trace mineral contents in ingredients are estimated to be zero

  ➔ Supplementation of trace minerals using premix meeting the overall requirement + safety levels

• Consequences for characterising bioavailability of minerals in diets

Bioavailability of native elements in basal diet

Bioavailability of premix elements

Overall bioavailability of elements in the diet
Influencing factors of bioavailability in animal nutrition with regard to trace minerals

- Dietary level
  - Ingredients
  - Feed additives
  - Amount of mineral supply
  - Physical properties
    - Particle size
    - Conditioning processes
  - Antinutritional factors
  - Feeding technique
  - Hygienic quality
  - Amount of feed intake

- Digestive level
  - Maturation gastrointestinal functions
    - Enzyme activity
  - Solubility of the sources
  - Microbiota
  - Redox potential
  - Health digestive disorders or disturbance

- Absorptive level
  - Electronic configuration
  - Chelating capacity
  - Interaction among minerals and nutrients
    - Homeostasis
  - Cellular transport

- Metabolic level
  - Animal species
  - Physiological state
  - Previous nutrition
  - Health status
  - Oxidative stress
  - Health status
  - Response criteria
    - Homeostasis
Homeostasis

Target: Maintaining cellular concentration gradients and substrate fluxes for achieving a physiological steady state
Instruments for homeostasis of trace elements

Intestinal tract

Intake → Absorption → Extracellular space → Endogenous secretion → Feaces

- Skeleton
- Organs
- Tissue

Storing → Blood

Mobilizing

Blood

- Urine
- Products

Functional forms
Measurement of bioavailability

➢ Traditionally
  • Typical or purified or semi-purified diets at deficiency levels of the tested mineral
  • Addition of the mineral source at graded levels
  • Measuring of response criteria
Levels of trace mineral deficiency

- Adequate
  - Resistance to diseases
  - Maximum productive and reproductive performance
  - Normal productive and reproductive performance
  - Clinical signs
  - Clinical
  - Impaired performance
Determination of mineral bioavailability

Response criteria

Support of normal performance

Dietary level of trace elements
Determination of mineral bioavailability

Response criteria

Support of normal performance

Amount depending on
- Choice of response variable
- Performance status
- Health status
- Environmental conditions and stress
- Pharmacological effects

Dietary level of trace minerals
Effects of response criteria on bioavailability of inorganic and organic trace mineral sources
Effects of inorganic and organic trace elements at recommended levels on Cu content in selected organs of post-weaning piglets at 47 d of age after a 14-day-depletion period (25 to 38 d of age)
Effects of recommended and overdose levels using inorganic (CuSO$_4$) or organic copper (Cu-Lys) on copper content in liver of post-weaning piglets at the end of a 42-day-feeding period.
Bioavailability used for comparisons of different mineral sources

- Bioavailability of a mineral in a particular source is determined relative to its functional availability from a standard source.
- Expression of bioavailability in terms of relative biological availability.
Potential parameters for characterising relative bioavailability of trace minerals (Jongbloed et al. 2002)

<table>
<thead>
<tr>
<th></th>
<th>Blood</th>
<th>Liver</th>
<th>Kidney</th>
<th>Bone</th>
<th>Enzyme activities</th>
<th>Health status</th>
<th>Performance</th>
<th>Absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Manganese</td>
<td>-</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Zinc</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Copper</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>
Relative bioavailability (Zn-content in tibia bone) of Zn-Met using different diet types in broiler chickens (Wedekind et al. 1992)

<table>
<thead>
<tr>
<th>Diet type</th>
<th>Relative bioavailability (%) of Zinc (ZnSO₄ x 7 H₂O = 100 %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purified diet</td>
<td>117</td>
</tr>
<tr>
<td>Semipurified diet</td>
<td>177</td>
</tr>
<tr>
<td>Corn-soybean meal diet</td>
<td>208</td>
</tr>
</tbody>
</table>
Effects of increasing Fe-intake on Fe-content in the liver of milk cows during lactation (Steinhöfel et al. 2012)
Effects of increasing Zn-intake on Zn-content in the liver of milk cows during lactation (Steinhöfel et al. 2012)
Effects of increasing Cu-intake on Cu-content in the liver of milk cows during lactation (Steinhöfel et al. 2012)
Effects of increasing Se-intake on Se-content in the liver of milk cows during lactation (Steinhöfel et al. 2012)

\[ P=0.095 \]
Relative bioavailability of zinc and copper sources for pigs (NRC 1998, Revy et al. 2003)

<table>
<thead>
<tr>
<th>Source</th>
<th>Relative bioavailability with respect to ZnSO$_4$ x 7 H$_2$O or CuSO$_4$ x 5 H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZnO (source 1 to 3)</td>
<td>55 - 87</td>
</tr>
<tr>
<td>ZnSO$_4$ x H$_2$O (source 1 to 3)</td>
<td>41 - 97</td>
</tr>
<tr>
<td>Zn-Met</td>
<td>77 - 120</td>
</tr>
<tr>
<td>Zn-Lys</td>
<td>79 - 110</td>
</tr>
<tr>
<td>Zn-Amino acids</td>
<td>100</td>
</tr>
<tr>
<td>CuO</td>
<td>0 - 10</td>
</tr>
<tr>
<td>CuCO$_3$ x Cu(OH)$_2$</td>
<td>60 - 100</td>
</tr>
<tr>
<td>Cu-Met</td>
<td>100 - 105</td>
</tr>
<tr>
<td>Cu-Gly</td>
<td>90 - 115</td>
</tr>
</tbody>
</table>
Possible reasons for inconsistent results evaluating relative bioavailability of trace minerals in diets for pigs and poultry

- Chemical properties
  - Mineral concentration
  - Ligands
  - Stoechiometry
  - Chemical structure
    crystalline / amorphous
  - Solubility
- Physical properties
  - Particle size distribution
  - Water absorption
- Experimental design
  - Depletion, repletion
  - Control (negative, positive)
  - Supplementation rate
- Response criteria used
- Diet composition
  - Purified or conventional ingredients
- Feed additives
  - Phytases, probiotics, organic acids
- Palatibility
- Physiological status
  - Breed
  - Age
  - Health
  - Performance
  - Stress
  - Mineral status
- Climatic conditions
- Hygienic conditions
Microscopical structure of different organically bound trace minerals (modified from Oguey 2007)

Zinc

Copper

Zinc

Copper
Effects of reduced premix addition by using inorganic trace minerals (Mn, Zn, Cu) on app. digestibility in broilers over a 35-day-feeding period

Native contents (calculated)
Mn: 41ppm  
Zn:  79 ppm  
Cu:  8.5 ppm

Normal inorganic premix using sulfates (ppm):
Mn 100, Zn 90, Cu 15

Premix using in amounts of
10% (Mn), 11.1% (Zn) and 67% (Cu) of the normal premix
Ratio of oxidized (dehydroascorbic acid) to reduced ascorbic acid (active antioxidant) in sows when fed inorganic and organic trace mineral sources at different levels (Peters and Mahan, 2004)
## Interactions among minerals

<table>
<thead>
<tr>
<th>Element</th>
<th>Typical antagonism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe</td>
<td>Ca, Cd, Cu, lignine, Ni, P, Pb, protein, phytate, Zn, sugar</td>
</tr>
<tr>
<td>Mn</td>
<td>Ca, Fe, Mg, P, phytate</td>
</tr>
<tr>
<td>Zn</td>
<td>arginine, Ca, Cd, Cu, Fe, Mg, Se, glucosinolates, P, phytate, S, Ni</td>
</tr>
<tr>
<td>Cu</td>
<td>Ag, Ca, Cd, Fe, Hg, Mo, P, Pb, phytate, S, Zn, Se</td>
</tr>
<tr>
<td>Se</td>
<td>As, Ca, Cd, Ag, Mg, Zn, Pb, Hg, Fe, S, Cu, J,</td>
</tr>
<tr>
<td>J</td>
<td>As, Ca, Co, F, glucosinolates, NO₃</td>
</tr>
<tr>
<td>Co</td>
<td>Fe, J</td>
</tr>
</tbody>
</table>
Upper limits for animal health and avoiding interactions among minerals (values in mg/kg DM)

<table>
<thead>
<tr>
<th>Element</th>
<th>Recommendation</th>
<th>Upper limits (88% TM)</th>
<th>Upper limits for animal health</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>EU 1334/2003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fe</td>
<td>50 - 120</td>
<td>750</td>
<td>500 - 1000</td>
<td>350</td>
</tr>
<tr>
<td>Mn</td>
<td>15 - 40</td>
<td>150</td>
<td>600</td>
<td>550</td>
</tr>
<tr>
<td>Zn</td>
<td>50 - 100</td>
<td>150 - 250</td>
<td>300 - 1000</td>
<td>100</td>
</tr>
<tr>
<td>Cu</td>
<td>4 - 15</td>
<td>15 - 35</td>
<td>20 - 100</td>
<td>50</td>
</tr>
<tr>
<td>Se</td>
<td>0.15 - 0.25</td>
<td>0.5</td>
<td>0.2 - 2</td>
<td>2</td>
</tr>
<tr>
<td>J</td>
<td>0.15 - 0.60</td>
<td>4 - 10</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>Co</td>
<td>0.20</td>
<td>2</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Mo</td>
<td>0.10</td>
<td>-</td>
<td>3 - 5</td>
<td>2</td>
</tr>
</tbody>
</table>
Conclusions

- Bioavailability of trace minerals in animal nutrition varies according to numerous factors at dietary, digestive, absorptive and intermediary level.
- Bioavailability varies according to the level of determination and the choice of response variables.
- The validity of bioavailability at present is only warranted when using standardized measurement conditions (minimizing homeostases, standard source and dietary effects, ……) and a specific response criteria.
- Bioavailability of native ingredients or typical basal diets of trace elements is scare and incomplete.
Thank you for your friendly attention!