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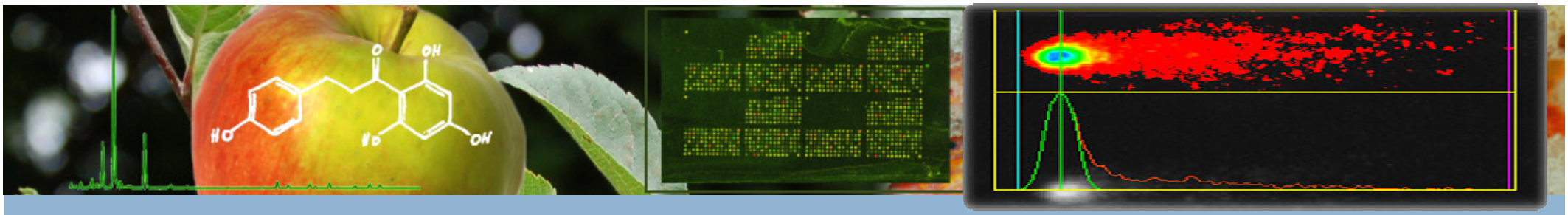

Definition of bioavailability from the viewpoint of human nutrition

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Bioavailability: Nutritional definitions

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Bioavailability – proportion of a nutrient that utilized/stored or available for utiliazation/storage

Bioavailability – **proportion** of a nutrient that is **digested/absorbed** and **metabolized trough normal pathways**. Forbes&Erdman, Ann. Rev. Nutr. 1983, 3, 213

In nutrition sciences the **bioavailability** of an essential metal is determined by its metabolic utilization. For this purpose the concept of "total utilization" defines the **fraction of a nutrient** that **is ultimately used in metabolism** after its digestion, absorption, and distribution. Schümann&Elsenhans, J. Trace Elem. Biol. 2002, 16/3, 139

Bioavailability is defined as „the **efficiency** with which a dietary component **is used systematically through normal metabolic pathways.**
It is expressed as a percentage of intakes and is known to be **influenced by dietary and host factors.** Aggett, Am.J.Clin.Nutr. 2010, 91(S), 1433S

Bioavailability – **proportion** of intake that is capable of being **absorbed trough/by the intestine** and made **available either for metabolic use or storage.** Lowe and Wiseman, J.Nutr. 1998, 128, 2809S

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Bioavailability: Nutritional definitions, Target system effects

The term bioavailability relates to the sum of impacts that may cause differences in degrees of deficiency states.

In nutritional science the term "bioavailability" encompasses the sum of impacts that may reduce or foster the metabolic utilization of a nutrient.
Schümann K et al., Arzneim.-Forsch./Drug Res. 47(I), 369-380, 1997

Bioavailability in this sense can be quantified by the rate by which deficiency symptoms are cured or by the weight gain during growth.

Bioavailability: Nutritional definitions

The concept bioavailability incorporates: (i) availability for the absorption or "bioaccessibility"; (ii) absorption; (iii) tissue distribution; and (iv) bioactivity.
Stahl et al., Molecular Aspects of Medicine, 2002, 23, 39

Once compound is absorbed it is inevitably bioactive, irrespective of whether or not it is chemically inert *in vivo*. Thus, the concept of bioavailability is not separate from but includes bioactivity. This proposal is built upon the following considerations:

*) Any compound that enters the „system" alters the concentration within the „pool", which will have an impact on the concentration in other „pools" and can therefore be considered bioactive (i.e. it has an impact on metabolism).

*) Pool concentration of a substance that exceeds the „threshold" (e.g. megadose of viatamin c) or substances are excreated unchanged because they cannot be metabolized or substances that are not biologically essential are bioavailable and thus bioactive, in that they have a metabolic impact, even if this is only the stimulation of detoxification processes, or the use of energy for their excreation.

Pharmacological definition used by nutritionists

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320.1 Definitions **FOOD AND DRUG ADMINISTRATION**
(Code of Federal Regulations; Title 21, Volume 5; Revised as of April 1, 2012)
The European Agency for the Evaluation of Medicinal Products

Bioavailability means the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and **becomes available at the site of action.**

Because of ethical and technical difficulties in accessing organ sites *in vivo* in humans the pharmacological definition has been redefined.

Bioavailability is understood to be the extent and the rate at which a substance or its active moiety is delivered from a pharmaceutical form and becomes available in the **general circulation** (EMA)

or

Bioavailability – fraction of an oral dose (parent compound or active metabolite) from a particular preparation that reaches the systemic circulation.
Schümann K et al., Arzneim.-Forsch./Drug Res. 47(I), 369-380, 1997

Bioavailability

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Processes:

Release of a nutrients from its matrix

Absorption of a nutrient into the systematic circulation

Distribution to the body‘s tissues

Metabolic utilization/storage in body

Excretion, the elimination of the compound or metabolite, from the body via renal-, bilary-, pulmonary processess.

Bioavailability is affected by many factors:

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Exogenous factors

Food matrix (raw; mechanical, thermal processing,..)

Chemical form of a nutrient (e.g. heme iron, non-heme iron,…)

Co-ingested compounds, which can increase or decrease solubility, absorption,..

(e.g., iron ± ascorbic, phytic acid,…)

Dosage

Endogenous factors

Nutrient status

Gastrointestinal disorders

Functional status of the gastrointestinal tract (production of digestive enzymes, bile,..)

Systemic factors (age, physiological state (pregnancy, lactation), genotype,.. .)

Liver and kidney function (metabolism, excretion,…)

Estimation of Bioavailability:
Nutritional studies:

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The balance method
Estimation of difference between ingestion of a nutrient (minerals) and fecal excretion. (apparent absorption) (intestinal balance).

Estimation of difference between sum of ingestion and secretion of a nutrient (minerals) and fecal excretion.

Urine increment method
Estimation of urinal excretion of a nutrient or nutrient metabolite in urine.

Tracer methods
Use of radioactive or stable isotopes.

Serum concentration
(AUC = **a**rea **u**nder the **c**urve) in the general circulation.
absolute bioavailability (if i.v. administration is possible):
F%= 100% x (AUCp.o. x Di.v.)/(AUCi.v. x Dp.o.)
relative bioavailability:
Fr%= 100% x (AUC_{test})/($AUC_{reference}$)

Target system effect
Rate by which a deficiency symptom is cured.

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Conclusions:

There are many different definitions of bioavailability in nutritional science. This should be taken as an indication of the complexity of the problem.

The correct estimation of bioavailability according definition – proportion of a nutrient that utilized/stored or available for utiliazation/storage- is hardly possible, yet.

There is often a discrepancy between definition and usage in the literature. The terms bioavailability and absorption are often used interchangeably.

The efficiency of bioavailability/absorption vary considerably depending on the conditions/factors (food matrix, co-ingested compounds, dosage, nutrient status, gastrointestinal disorders, pregnancy, lactation,..) It is necesary to estimate bioavailability/absorption at strictly standartized conditions/factors.

Definition of bioavailability - the rate by which `deficiency symptoms` are cured - is applicable only for few essential nutrients and when there is no deficiency of another nutrients which are important for these `deficiency symptoms`.

If there are substantial impacts of homeostatic mechanisms on the plasma concentration of a nutrient, the pharmacological definition and estimation of bioavailability is difficult to applicate.