Introduction to Methodology for Risk Assessment for Nutrients for Promoting Public Health-Safety/Benefits

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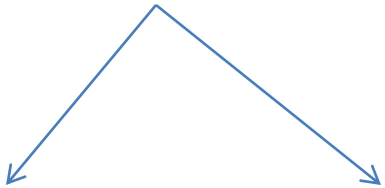
Food Risk Assessment



Chemical

Additives, Pesticides

Environmental Contaminants

Microbiological

Pathogens

Impact of Poor Quality diets

High intake of Salt ,Sugar and Saturated Fat

Salt	Above 5g/day
Saturated Fat	Above 22g/day (2000kcal diet)
Sugar	Above 25/day (2000Kcal diet)

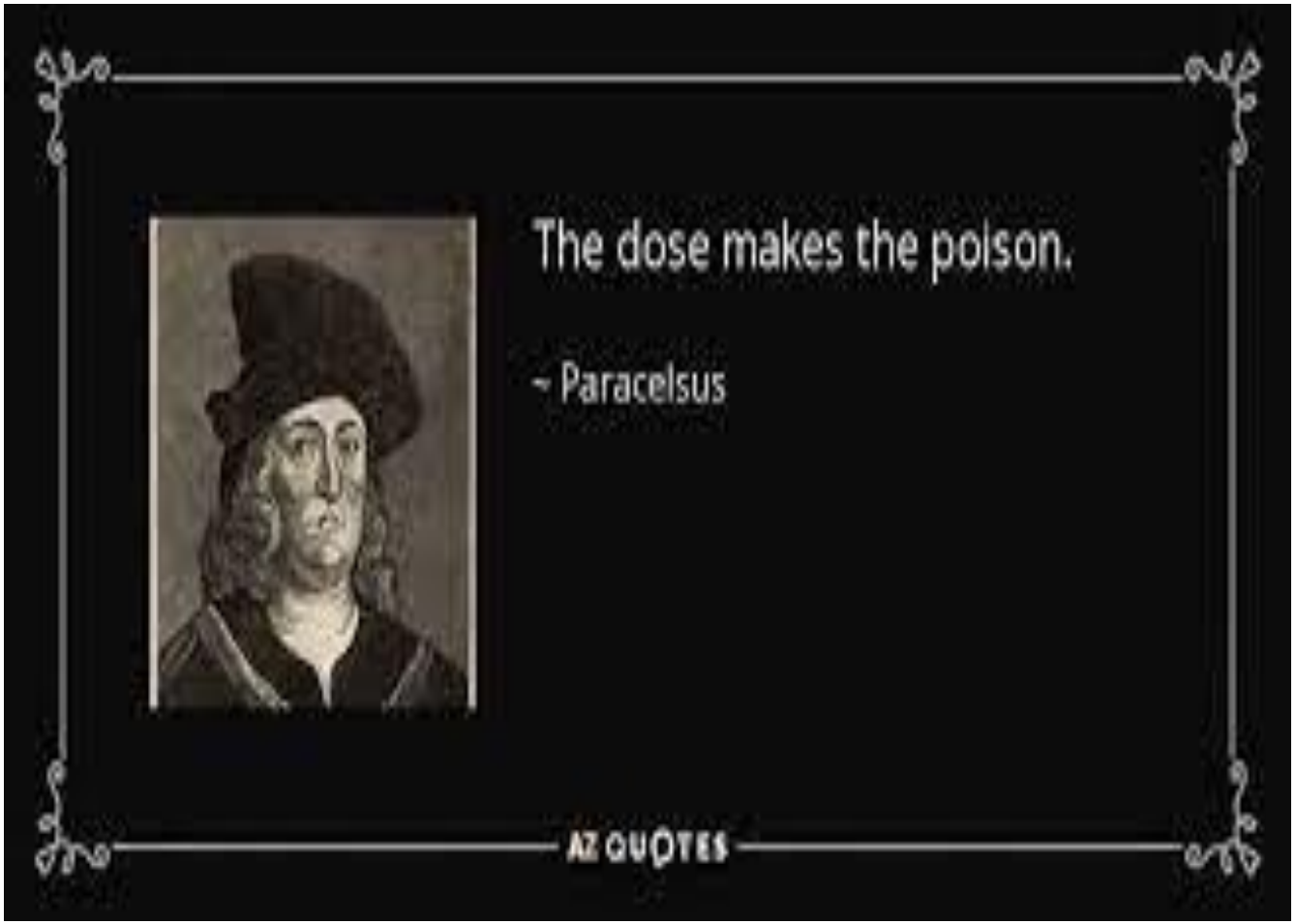
Inadequate intake of Micro nutrients – Subclinical deficiencies

Risk Assessment of Nutrients

Dietary supplements – Vitamins & Minerals

Food fortification -mandatory & Voluntary

Concern on the excessive and regular consumption



First rule of Toxicology


RISK = HAZARD x EXPOSURE

Risk Assessment Method

Risk Assessment in Federal Government: Managing the Process (NRC 1983)

Risk Assessment

Hazard Identification

Hazard Characterization

Exposure Assessment

Risk Characterization

Additives : Hazard Identification and Characterization

Initial toxicity studies -Absorption, distribution, metabolism and excretion(ADME)

The selection of appropriate test species and test doses for toxicity studies

Short-term and long-term tests for general systemic toxicity
Identify target organs for toxicity and may indicate the need for additional or more specific testing (e.g. for neurotoxicity or immunotoxicity)

Rodent and Non Rodent or Two rodent species in both males and females to maximize the opportunity to find adverse effects. Testing -best relates to
human exposure scenarios – diet, gavage or water
OECD guidelines and Good Laboratory Practices

Hazard characterization

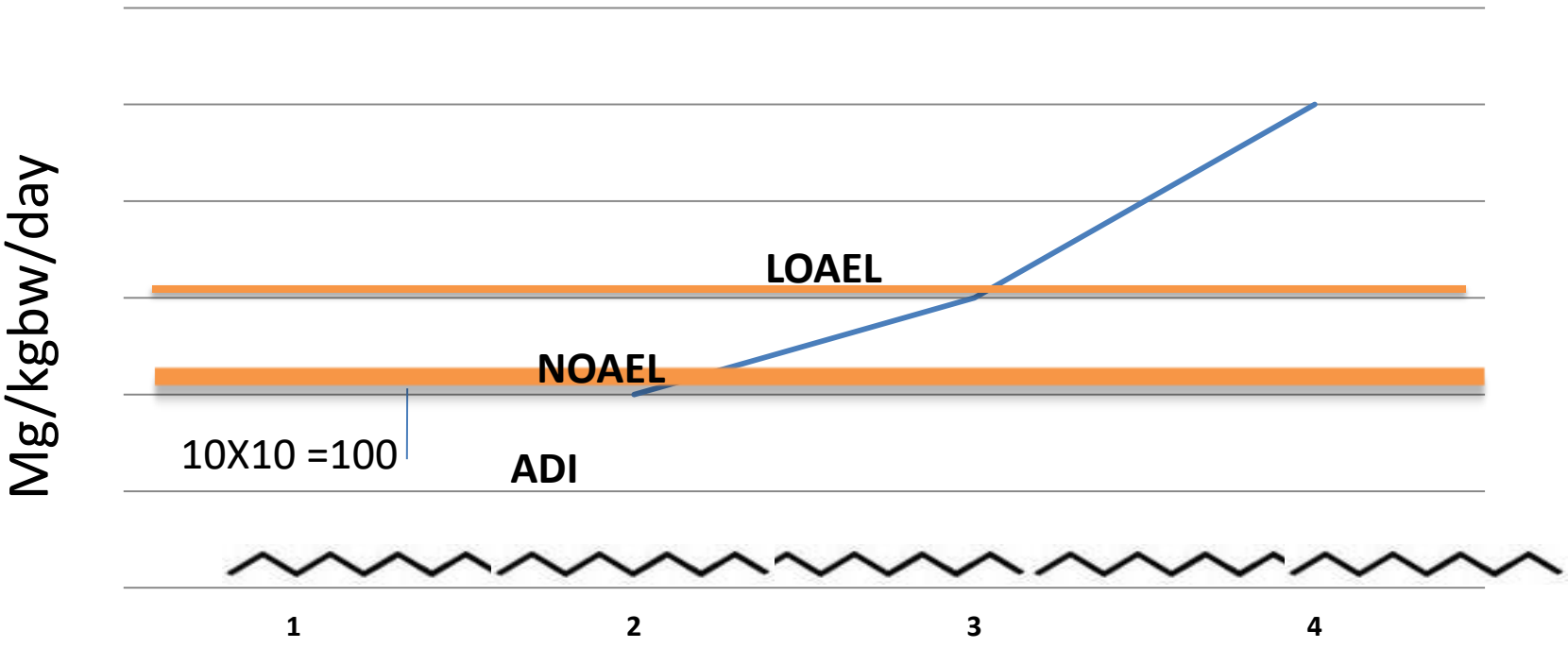
Dose response data – Identify Lowest Observed Adverse Effect Level
& No Observed Adverse Effect Level

Most relevant endpoint
Most sensitive species NOAEL
Safety /uncertainty factor -extrapolation
Test species to humans 10
Possible human differences in response 10
10x10 ADI = NOAEL/100 = X mg/kgbw

Acceptable Daily Intake

The Acceptable Daily Intake (ADI) is an estimate by JECFA of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk (standard man - 60 Kg) (WHO 1987). The ADI is expressed in milligrams of the additive per kilogram of body weight. For this purpose, "without appreciable risk" is taken to mean the practical certainty that injury will not result even after a life-time's exposure (Report of the 1975 JMPR, TRS 592, WHO, 1976).

Relation between ADI, NOAEL and LOAEL



Half life is short -No cumulative toxicity expected

Application of Risk Assessment Method to Nutrients

Nutrients	Food Additives
Threshold chemicals	Threshold chemicals
Dual risk	On risk
Homeostatic mechanism	No homeostatic mechanism
Metabolic, physiological differences by age, sex & life stage	Not as general consideration
Tolerable Upper level vary with age, sex & life stage	Acceptable Daily intake is always milligram/KG body weight

Steps in Risk Assessment

Step 1. Hazard identification –This step involves in identifying the known or potential adverse health effects of a given nutrient. It involves collecting, organizing, and evaluating all information about a given nutrient's adverse effects.
This section concludes with a summary of the evidence regarding the nutrient's potential to cause adverse effects in humans.

Step 2. Hazard characterization – This step is the qualitative and quantitative evaluation of the nature of the adverse effects associated with a nutrient; this includes a dose-response assessment, i.e., determining the relationship between nutrient intake (dose) and identification of adverse effects (in frequency and severity). A UL is derived from these evaluations, taking into account the scientific uncertainties in the data, with different ULs that may be derived for various life-stage groups.

Tolerable Upper Intake Level (UL)

The Tolerable Upper Intake Level (UL) refers to the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population.

As intake increases above the UL, the risk of adverse effects increases.

Highest Observed Intake(HOI)

Highest Observed Intake is an alternative approach to the derivation of UL. This approach was proposed in 2006 at the FAO/WHO Technical Workshop on Nutrient Risk Assessment (FAO/WHO, 2006)

for use when there is little NOAEL or LOAEL data upon which to conduct a risk assessment is to establish the Highest Observed Intake (HOI), derived only when no adverse health effects have been identified.

"It is the highest level of intake observed or administered as reported in studies of acceptable quality."

Observed Safe Limit (OSL)- Term proposed by Hathcock (2004)

Step 3. Exposure assessment-This step- evaluates the normal daily nutrient intakes of the general population.

Step 4. Risk characterization -This step analyses the conclusions from steps 1 through 3 and characterizes the risk. Generally, the risk is considered the probability of an adverse effect (and its severity). Risk will be proportional to the proportion of the population that exceeds the UL and the magnitude and duration of the excessive consumption. The scientific uncertainties associated with the UL and intake estimates are described during risk characterization so that risk managers know the level of scientific assurance they can place in the risk assessment.

Critical End points used in determining the ULs

IOM			EFSA
Vitamin A	Adults	Liver abnormalities	Teratogenicity
	Women in reproductive age	Teratogenicity	
	Infants	Fontanel bulging	
Vitamin C	All ages	Osmotic diarrhea	Not considered as there was no dose response
Iron	All ages	Nausea, vomiting	It was considered as transient effect

Application of Uncertainty factors

Large UF 100 (Additives and Pesticides)

Extrapolation from Animal Studies and large UF for Nutrient will go below the requirement

Small UF 1-10

Mostly Human studies

UF depends on

1. Extrapolation from animal to Humans

2. Short term exposure is used rather long term

3. Small number of subjects used in experiments

4. Greater severity of hazard

5. Using LOAEL rather than NOAEL

   (11 Uls are based on LOAEL)

Different UFs for Same Critical End Point

Nutrient	IOM	EFSA
Copper	2	1
Vitamin E	36	2
Boron	30	100

Chronic Disease Risk Reduction Intake Model

Shift of public health burden

Deficiency Diseases → Chronic Diseases

Chronic diseases –complex, multifaceted &
develop over a time period

DRI lacked the mechanism for evaluation
for evaluating evidence

Cause, Intake –Response between Nutrient intake and Chronic Disease

Guiding Principles Report (NASEM 2017) Recommendations

11 Recommendations

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Method

To retain Uls based on traditional toxicity end point
But if, increased intake of nutrient increases the risk, such relationship range should be characterized to indicate where a decreased intake is beneficial

Sodium CDRR intake

Population	Age group (yrs)	Sodium mg/day
Children	1-3	1200
Children	4-8	1500
Children	9-13	1800
Children	14-18	2300
Adults	≥ 19	2300

Revised AI values for Potassium*

Males	AI mg/day (2005)	AI mg/day (2019)
9-13yrs	4500	2500
14-18yrs	4700	3000
19-30yrs	4700	3400
31-50 yrs	4700	3400
51-70 yrs	4700	3400
> 70yrs	4700	3400

*** After application of CDRR Model**

in conclusion

1. UL is meant to be used as a guidepost for potential adverse effects of nutrients and to help ensure that individual intakes do not exceed a safe intake or do so only rarely

2. Critical input for NRA would be the accurate nutrient intake data from all sources ie food, fortified food & supplements.

3. Chronic Disease Risk Reduction intake model is new category in DRIs

Thank you for your attention