EFFICACY AND SAFETY OF FOOD ADDITIVES

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Definition of Food Additive

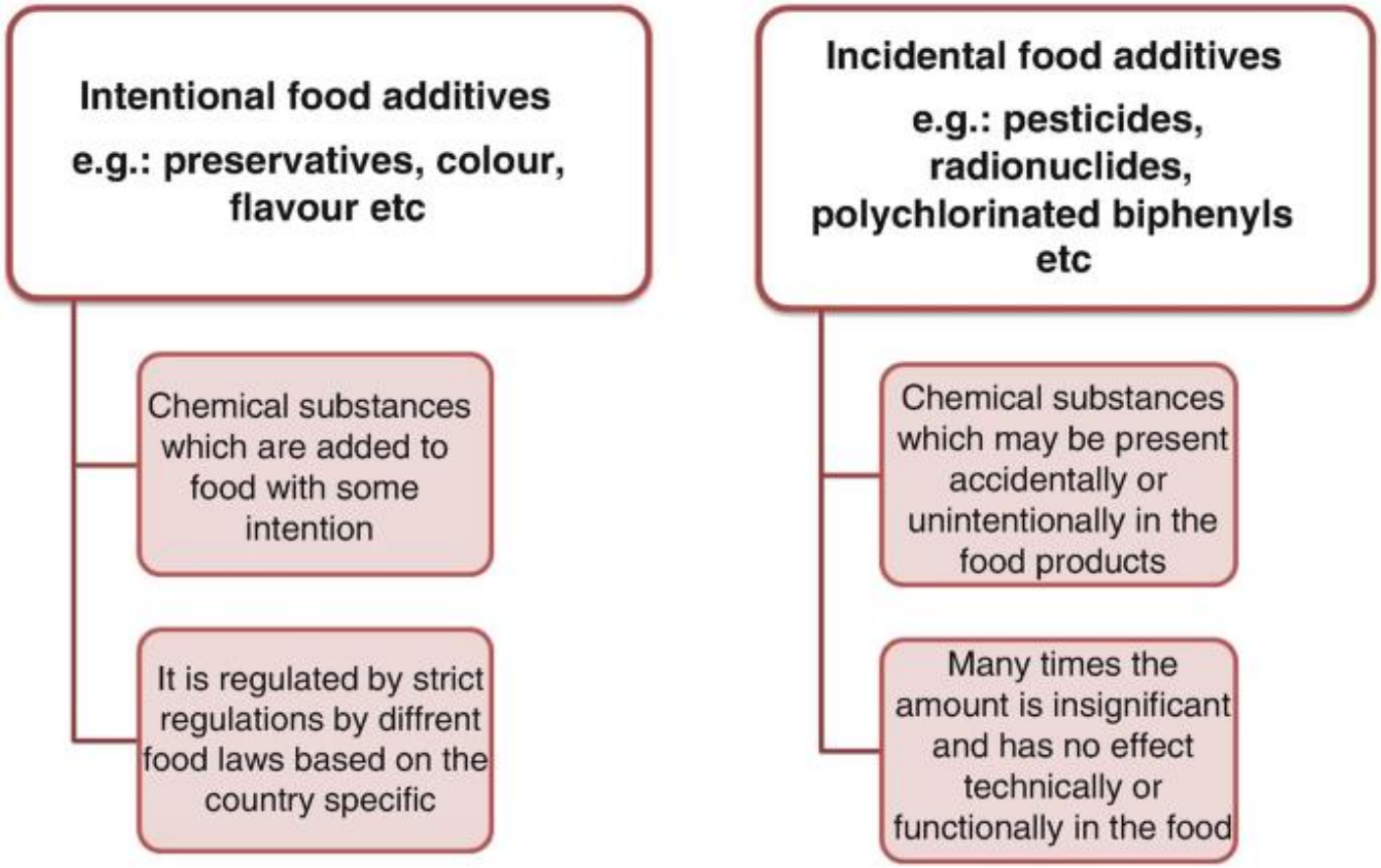
Food Additive means… Substance not normally consumed as a food by itself or used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition for a technological purpose (including organoleptic) in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result (directly or indirectly), in it or its by-products becoming a component of or otherwise affecting the characteristics of such food but does not include “contaminants” or substances added to food for maintaining the nutritional quality….

Food Additive is a substance not normally consumed as a food but added to food for a specific technological purpose.

Does not include “contaminants” or substances added to food for maintaining or improving nutritional qualities.

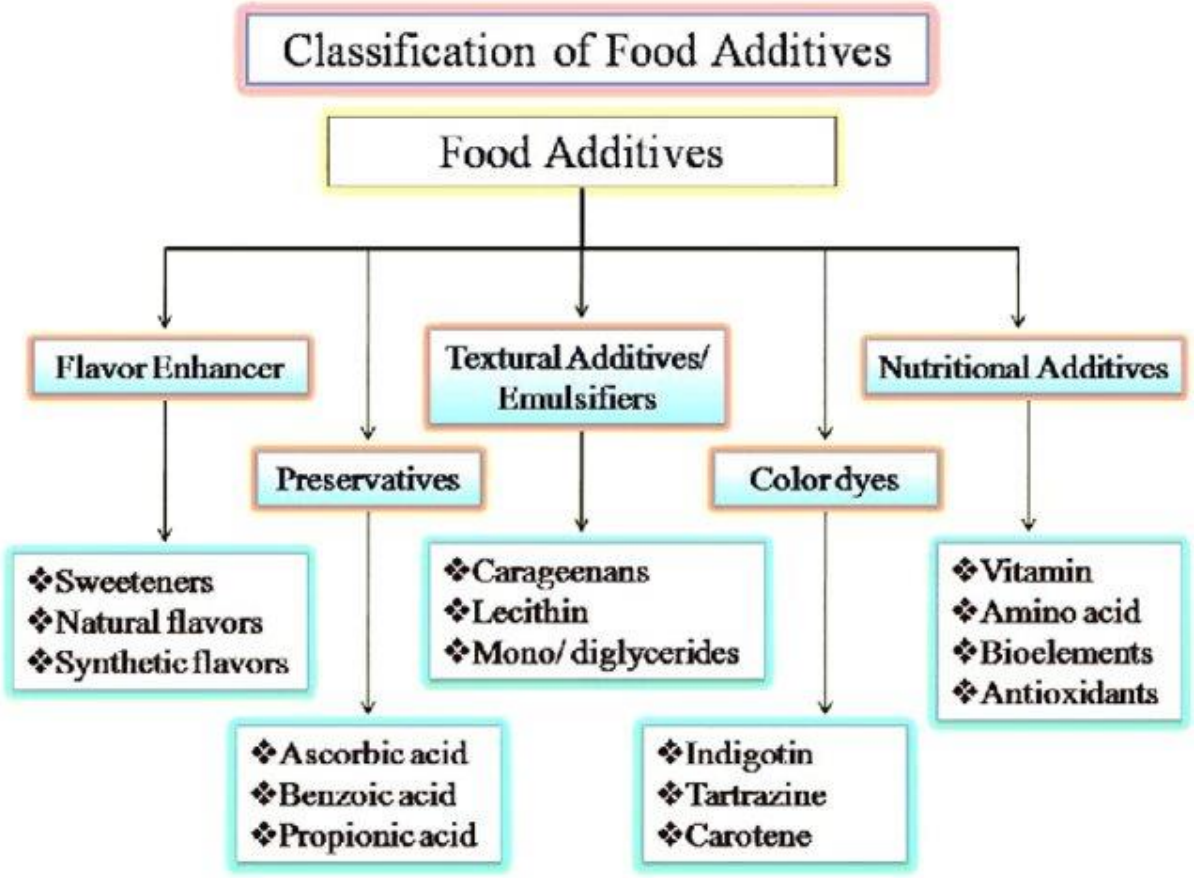
- Food is a very common source of toxicant exposure to humans.
- An unknown number of naturally occurring contaminants find their way into food.
- The most ominous are products of mold growth called mycotoxins
- On the other hand, more than 2500 chemical substances are added to foods to modify or impart flavor, color, stability, and texture, to fortify or enrich nutritive value, or to reduce cost.
- In addition, an estimated 12,000 substances are used in such a way that they may unintentionally enter the food supply.
- Additives are not considered “nutritional” even if they possess nutritive value.

Intentional Vs. Incidental food additives



doi.org/10.1007/978-981-19-4796-4_7

Groups of Food Additives



10.1007/978-981-19-4796-4_7
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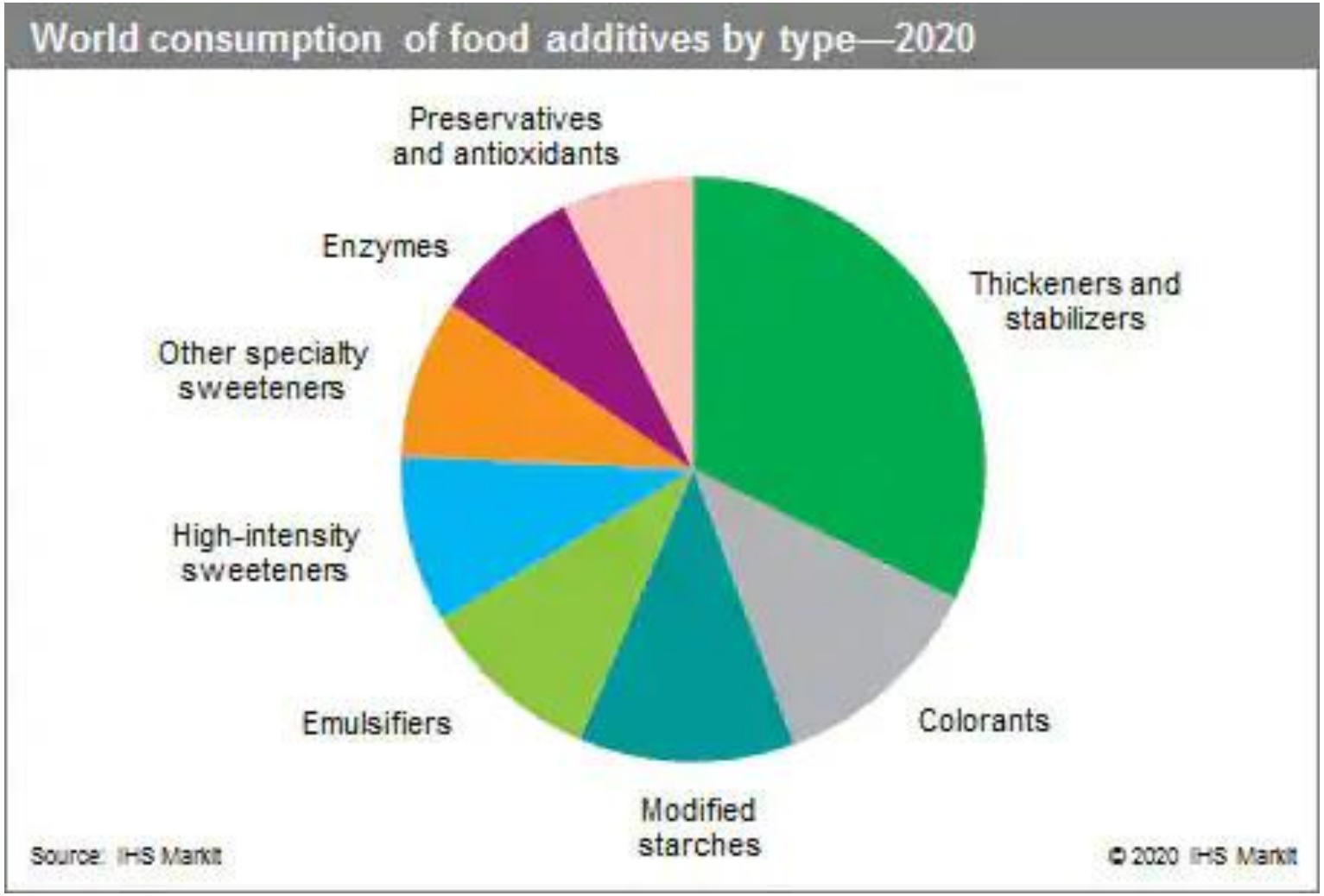
Food additives Functional Classes and Uses

Functional Class	Function / Technological Purpose	Example
Acidity Regulator	Controls acidity or alkalinity for safety and stability of foods	Citric acid
Thickener	Increases the viscosity of food, Provides body, texture and binding	Vegetable gums in soups
Anticaking agent	Free movement /flow of particles	Table Salt
Carbonating agent	Provide carbonation in water	Used in Cold drinks
Carrier	Dilute/Disperse food additive/nutrient without altering function to facilitate handling, distribution	Carrier, Diluent and encapsulation
Sweeteners	intense sweetness imparting ingredients to reduce sugar addition in foods	Steviol Glycoside, Sucralose in foods
Antifoam agent	Reduces foaming	Polydimethylsiloxane
Bulking agent	Add bulk without contributing significantly to its available energy value	Fillers, Polyols
Colour	Add or Restore color in a food	Colours, Decorative agent

Food additives Functional Classes and Uses

Functional Class	Function / Technological Purpose	Example
Emulsifiers	Maintains uniform emulsion of 2 / more phases in a food	Clouding agent, Emulsifier (Lecithin),
Flavour enhancer	Enhance existing taste/flavour without imparting flavor of their own	Soups
Gelling agents	Gives texture through formation of gel	Pectin in jams
Preservative	which prolongs the shelf-life of food by protecting against deterioration caused by microorganisms / prevent mold and bacteria from spoiling food	Benzoate in Beverage, Nisin in cheese, Nitrate /Nitrite in cured meat, SO2 in Table Sugar
Raising agents	liberates gas to increase volume of a dough or batter	Baking powder in bakery
Stabilizers	Maintain uniform dispersion of components / prevents separation	Carragenean in dairy based drinks

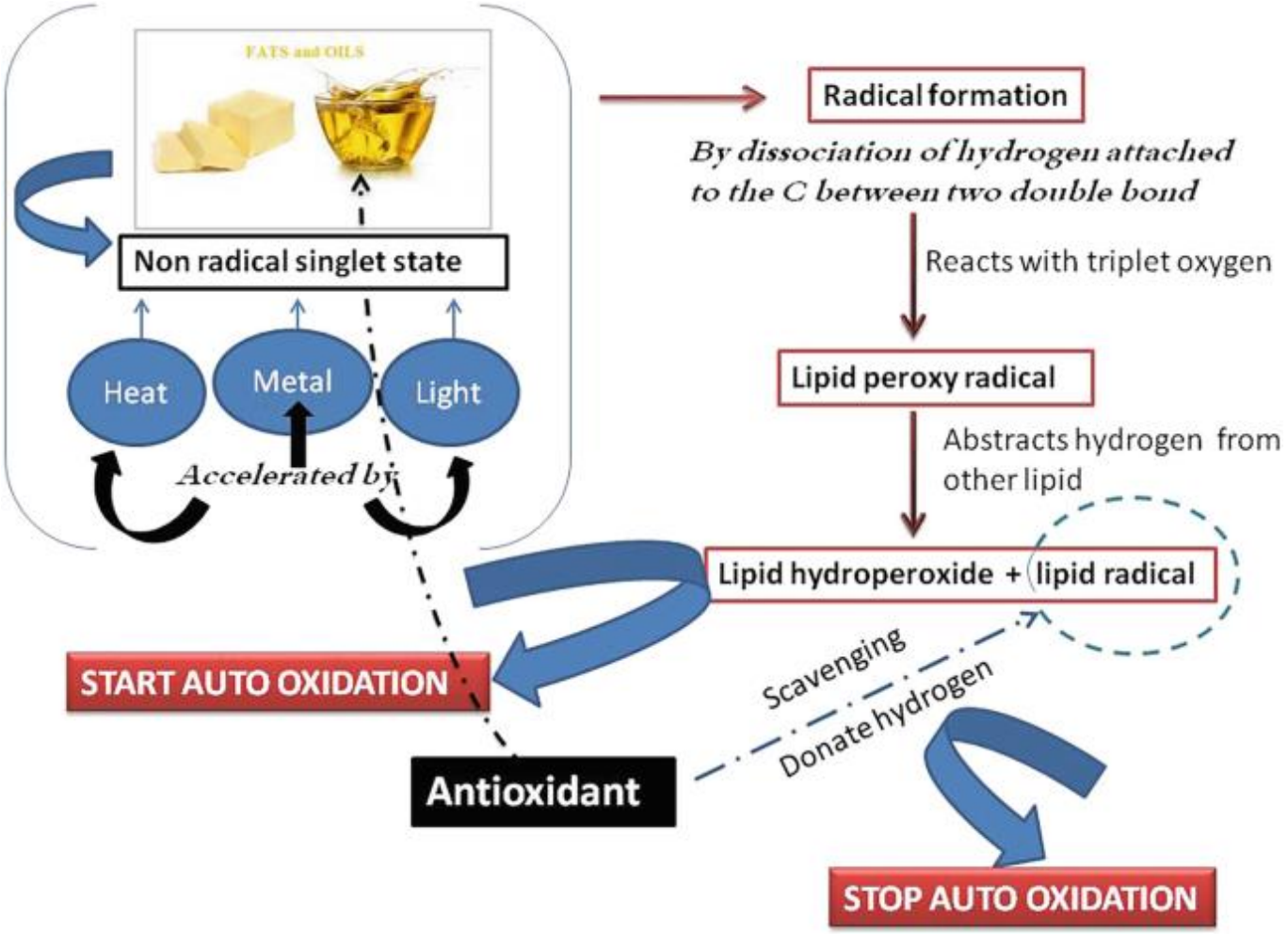
etc.....

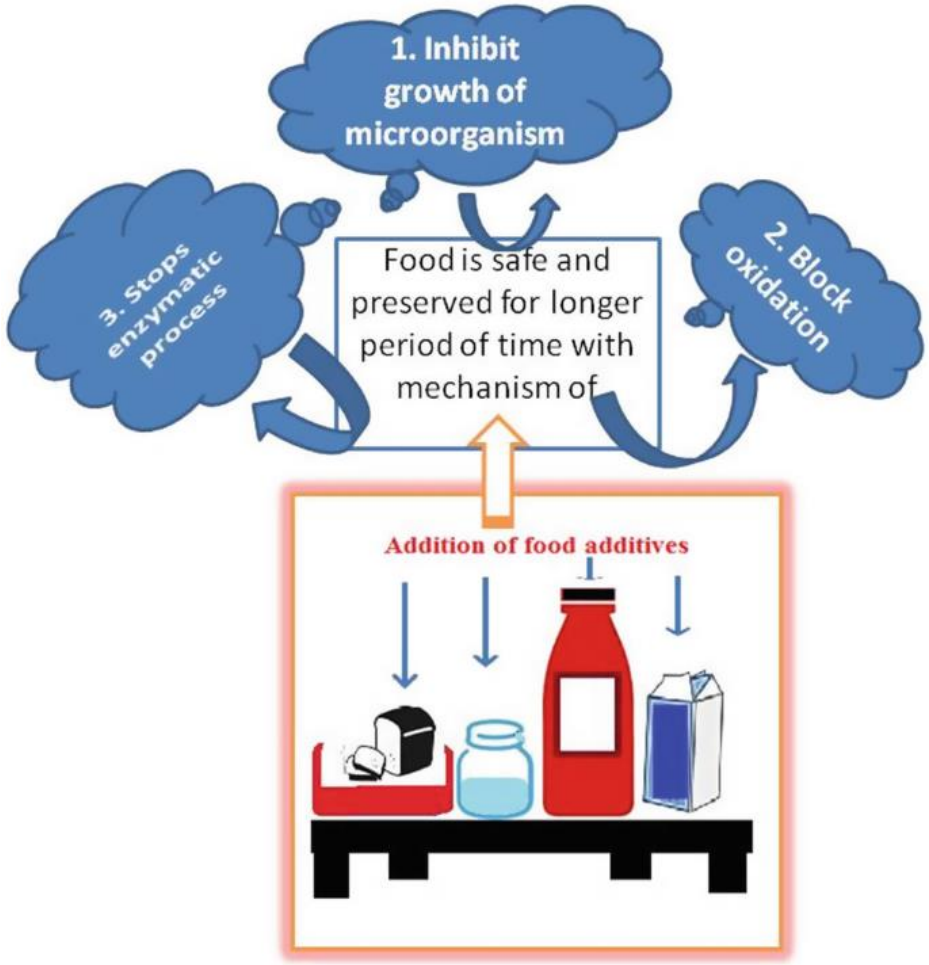


https://www.spglobal.com/commodityinsights/en/ci/products/chemical-food-additives-scup.html

http://14.139.62.46:8888/focus/
Accessed on 5th march 2024

Efficacy of Additives, few examples





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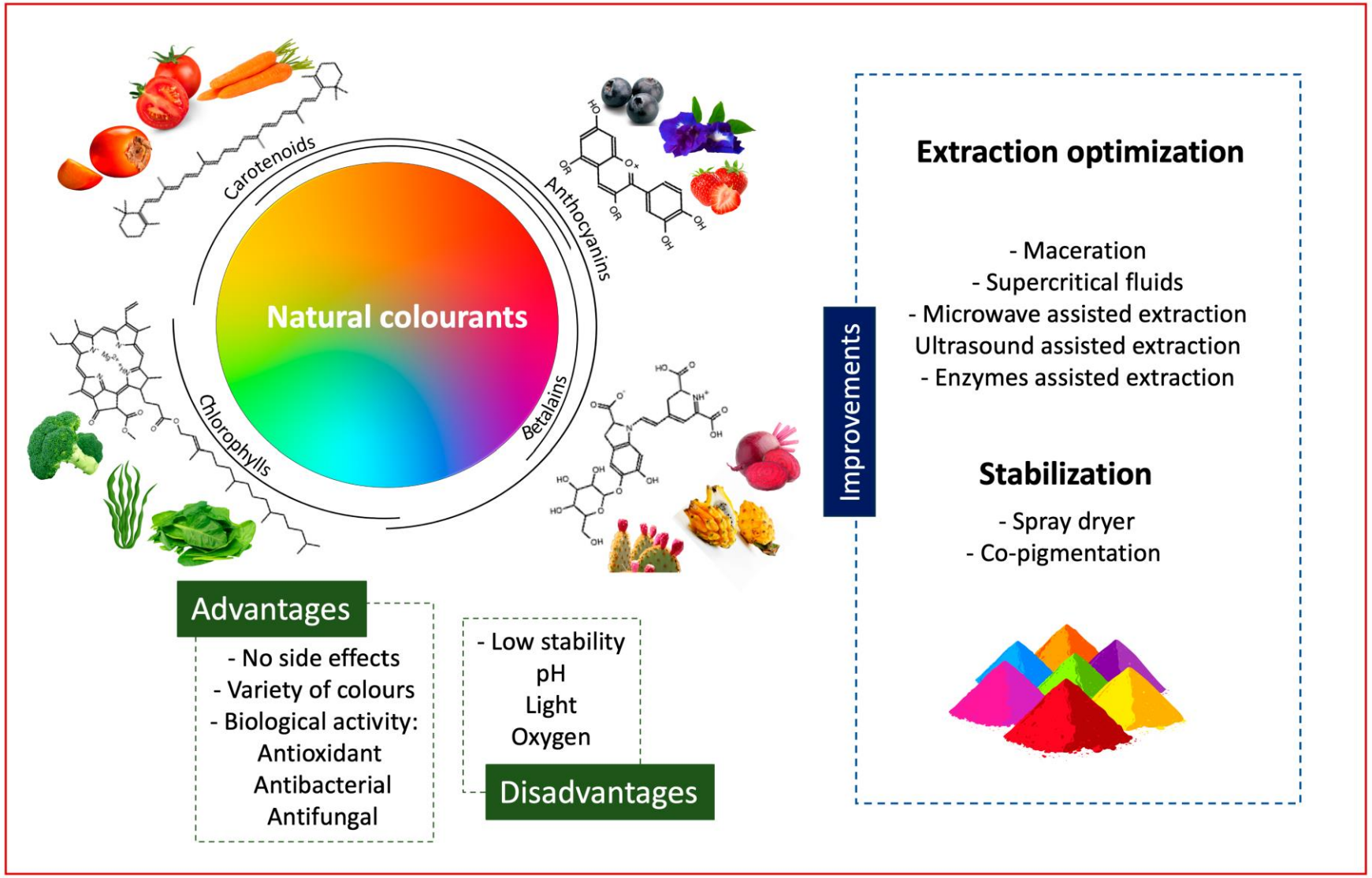
Food Colorants



10.3390/foods12224102

Focus Database
Food Additive Database

Food Additives Collected (3791)

U.S. Food and Drug Administration website

Searched for .sdf files

Natural Food Additves

Searched For Natural Source

Food Additives (2885)

18 Categories

1. Acidity regulators
2. Anticaking agents
3. Antimicrobial agents
4. Antioxidants
5. Boiler water additives
6. Colors
7. Dough conditioning agents
8. Emulsifers
9. Enzymes
10. Fermenting aids
11. Firming agents
12. Flavor enhancers
13. Masticatory substances
14. Nutrition enhancers
15. Preservatives
16. Solvents
17. Sweeteners
18. Others

Identifiers, Physiochemical Properties, 2D Structure Collection

Searched For

- ADI Values
- GHS Siginals
- Biological Pathways

ADME and Toxicity Prediction

Physiochemical Properties : Molecular Weitght, HBA, HBD, No of rotatable bonds, Topologica1 , Polar Surface Area.

ADME Properties : HumanIntestinal Absorption, Aqueous Solubiligy Level, Plasma Protein Binding Level, Blood Brain Barrier Penetration, CYP2DE Binding Level, Hepatotoxicity Level.

Toxicity Properties : Carcinogenicity: NTP Prediction/FDA Prediction , TD_{50} (Mouse), TD_{50} (Rat), LD50 (Rat Oral), LC_{50} (Rat Inhalational), Rat Chronic LOAEL, Developmental Toxicity, Mutagenicity (Ames), Skin Irritancy, Skin Sensitization, Ocular Irritancy, Aerobic Biodegradability.

Risk assessment

- Where the human food matrix and eating is concerned, the tasks of hazard and risk assessment become complicated almost in exponential fashion.
- Variation in dietary patterns, lifestyle, age/stage of development, gender, genotype, physiology, and pathophysiology may represent significant confounds.
- Toxicokinetic and toxicodynamic studies reveal that different dose levels and interactions with other nutrients and bioactive moieties can produce varying responses in factors such as stability, solubility, absorption, protein binding, and metabolism of the additive in question

https://www.slideshare.net/JasmineJuliet/types-of-food-additives-235616184

The Redbook – safety assessment

- 4 basic principles for safety assessment of food additives:

1) the agency presumes that some toxicological information is necessary for every food additive.

2) the amount of safety data required for a particular food additive is dictated by what is called a level of concern (LOC).

3) LOC is based on the magnitude of potential human intake of an additive and its molecular structure: exposure data, if available, carrying greater weight than the structure alert.

4) Initial evaluation of testing requirements can be adjusted when the data suggest that a significant or unexpected adverse effect is found to be associated with the ingestion of a particular additive.

The results from toxicology studies are then utilized to calculate an acceptable daily intake (ADI) which is compared to the estimated daily intake (EDI). If the EDI is less than the ADI, the additive is determined to be safe under the proposed conditions of use.

Level of Concern: Direct Food additive

Predictive measure of the likelihood that a hazard presented by a particular additive may result in harm.

CL I compounds require a short-term feeding study (at least 28 days in duration) in a rodent species and short-term tests for carcinogenic potential.
CL II requires testing in a 90-day feeding study in a rodent and a nonrodent species, a multigeneration reproduction study with a developmental toxicity phase, and a battery of short-term tests for carcinogenic potential.
CL III compounds are required to undergo more extensive testing, in addition to the studies required for a CL II substance, carcinogenicity studies in two rodent species, and a chronic feeding study of at least 1 year in duration in a nonrodent species.
These testing requirements are subject to modification based on the available data.

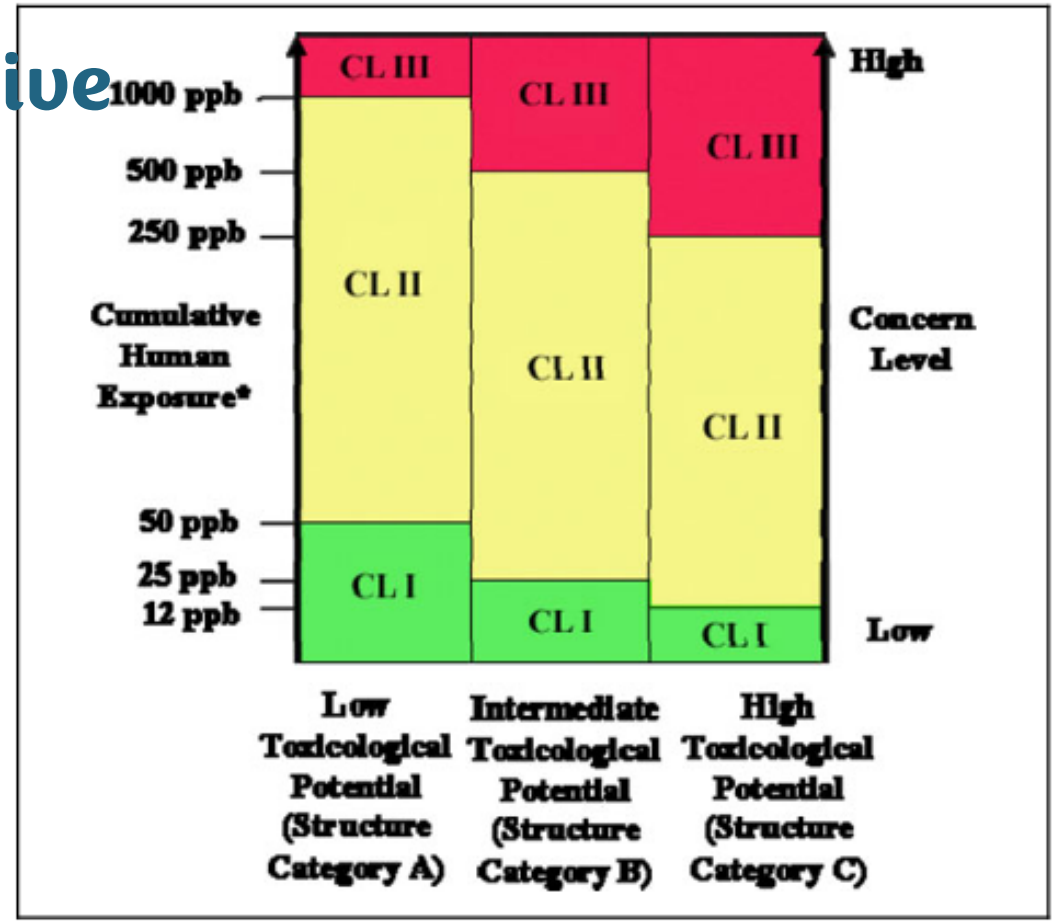


Figure 1. CLs as related to human exposure and chemical structure. *Cumulative human exposure is expressed as parts per billion (ppb; equivalent to microgram per kg diet) of daily dietary consumption of additives. Conversion of ppb to microgram per kg-body weight per day, divide by 20, assuming 3-kg daily diet (From US FDA Redbook[6]). CL: concern levels; FDA: Food and Drug Administration.

EDI (Estimated daily intake)

- The EDI is determined by multiplying the dietary concentration of the additive by the total weight of food consumed by an individual per day (3000 g). For direct additives, the concentration is the amount recommended for each of the additive's technical applications.

- The EDI is used together with information on exposure from all other uses of the indirect additive to establish the CEDI which is used to establish the level of toxicological testing recommended.

Toxicology testing in animals

The extent and types of toxicological studies required to support the safety of either direct or indirect food additives are dependent on both the EDI and the expected nature and potential for toxicity of the additive. This includes:

- *Short-term genetic toxicity studies*
- *Acute oral toxicity studies*
- *Short-term feeding studies*
- *Sub chronic feeding studies*
- *Reproductive and developmental toxicity studies*
- *Chronic toxicity and carcinogenicity studies*
- *Human data (clinical studies)*
- *Environmental effects of food additives*

Risk Assessment

Acceptable daily intake:

An ADI for human consumption of food additives, as accepted worldwide, is calculated as follows:

- Most sensitive indicator (noncancer effect) of toxicity (point of departure) is identified.
- Threshold or highest NOAEL is identified for the effect.
- The NOAEL is divided by safety factors to arrive at the ADI.

From NOAEL to Establishing Acceptable Daily Intake an Example:

Acceptance Daily Intake (ADI)=amount "that can be ingested daily over a lifetime without appreciable health risk" (WHO 1987).

Based on No-Observed Effect Level (NOAEL)

- from long-term studies in 2-3 species
- use most sensitive species

Apply "safety factors" of 100 to account for:

- differences between individuals (10 X)
- differences between humans and animals (10 X)

NOAEL/safety factor = ADI (mg/kg/day)

For example:

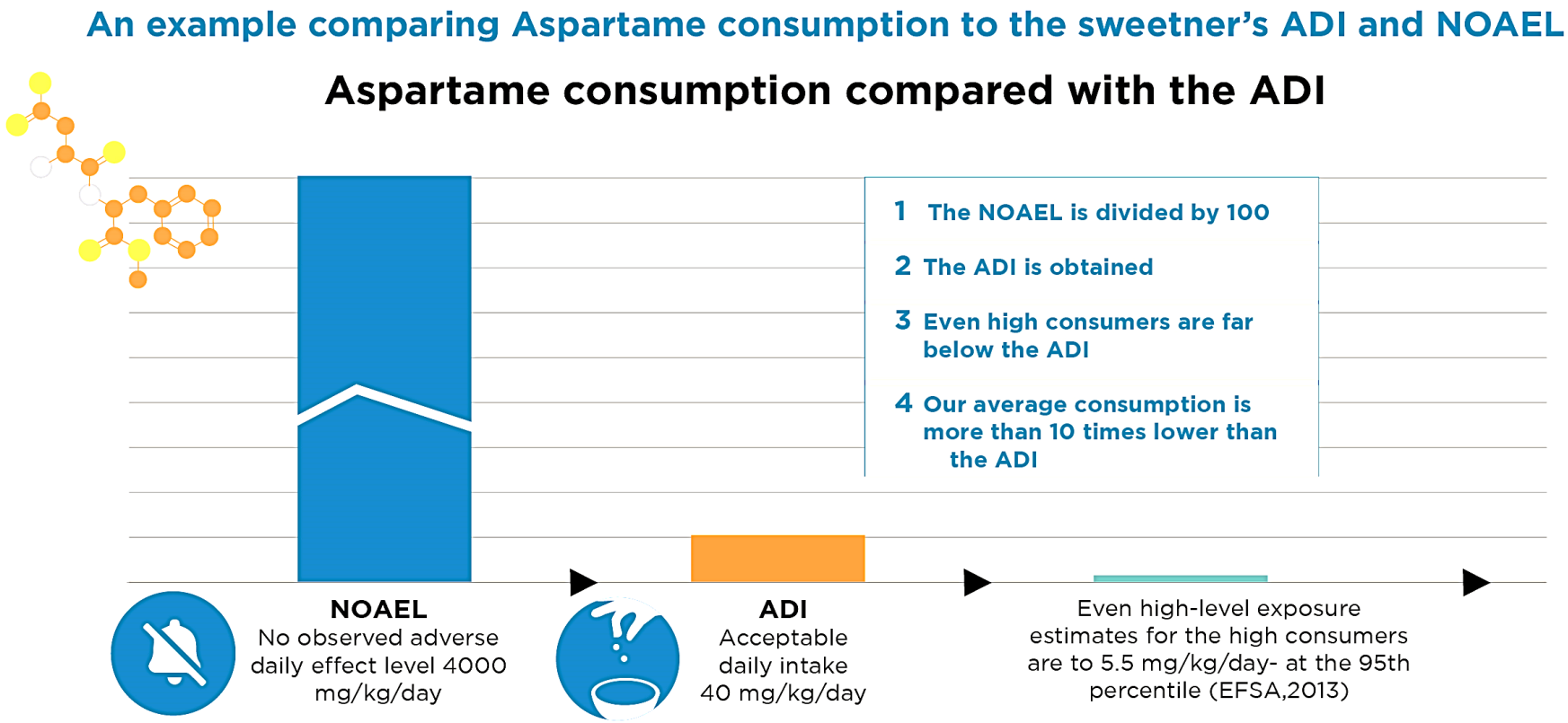
NOAEL = 4000 mg/kg/d,

ADI = 40 mg/kg/d.

ADI is very conservative, based on level with no effect when fed to animals for life-time and divided by "safety factor" cushion.

Reference: Bernadene A. Magnuson, Michael C. Carakostas, Nadia H. Moore, Sylvia P. Poulos, Andrew G. Renwick, Biological fate of low-calorie sweeteners, *Nutrition Reviews*, Volume 74, Issue 11, November 2016, Pages 670–689, https://doi.org/10.1093/nutrit/nuw032

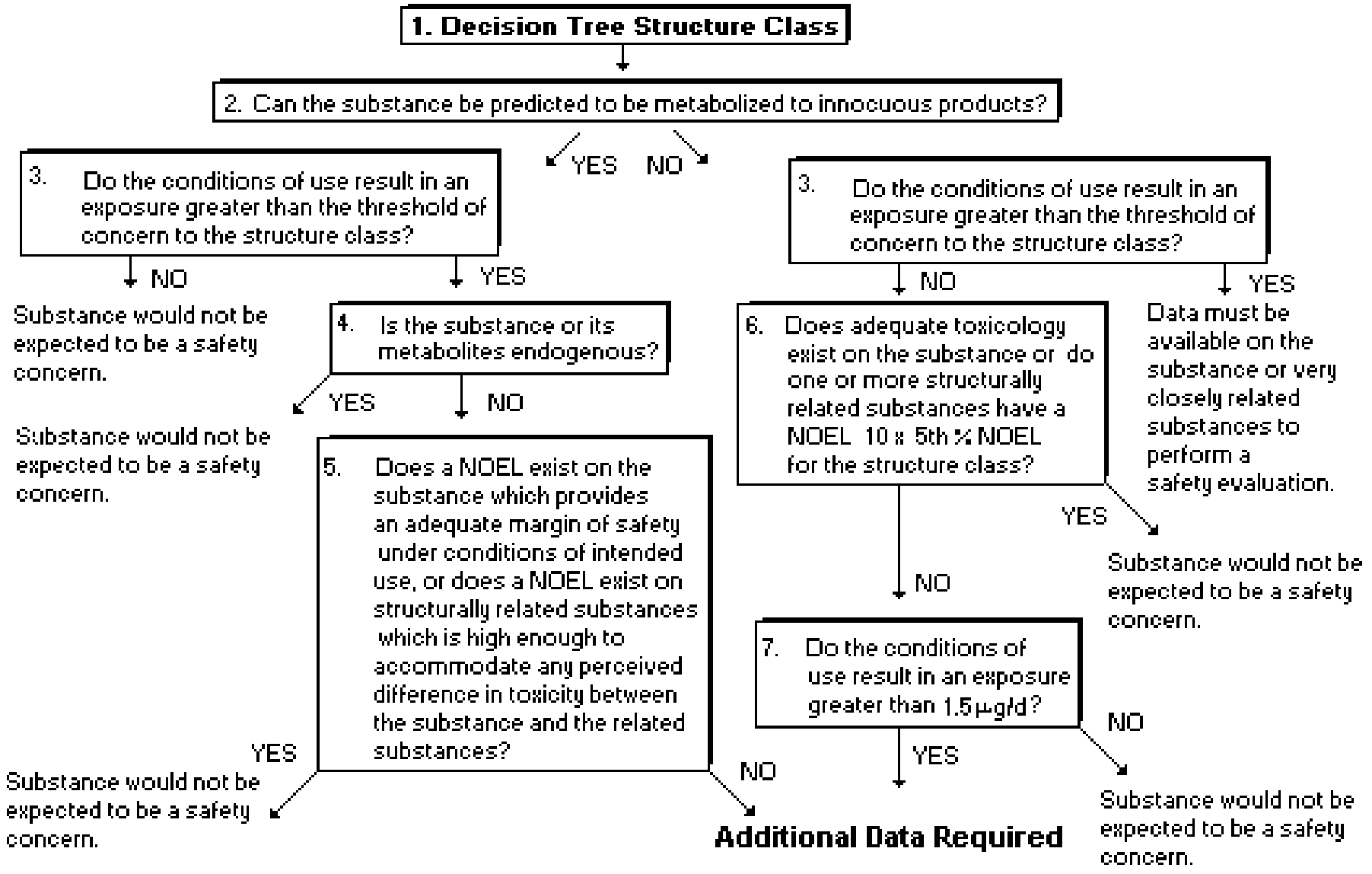
An example comparing Aspartame consumption to the sweetener's ADI



Aspartame consumption (EFSA, 2013) compared to the sweetener's Acceptable Daily Intake (ADI) and no observed Adverse Effect Level (NOAEL)

Reference: https://www.sweeteners.org/resources/

Figure 2 Safety Evaluation Sequence



https://inchem.org/documents/jecfa/jecmono/v35je21.htm

SUGAR
FREE

SALT
FREE

CAFFEINE
FREE

GMO
FREE

CARB
FREE

GLUTEN
FREE

LACTOSE
FREE

PESTICIDE
FREE

CALORIE
FREE

LECTIN
FREE

PARABEN
FREE

PALM OIL
FREE

Thanks

UNFORTUNALTY NOT
FOOD ADDITIVE FREE