

Absorption of Toxicants

Food Toxicology

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Learning Objectives

- Describe the ways in which toxicants interact with cells.
- Recognize how the molecular characteristics of toxicants affect entrance into a cell.
- Explain human anatomy as related to integumentary, respiratory and digestive systems.
- Summarize the routes of toxicant absorption.

Organization of the Body

Metabolism: Molecular Organization

Composition of Bacteria

Cell Structure

The Cell

Proteins

- Synthesized primarily during a process called translation.
- Building blocks of proteins are amino acids.
- Proteins are made of a long chain of amino acids
 - Peptide bonds; disulfide bonds (Cys).
 - Primary structure is sequence.
- Sometimes modified by:
 - Heme, sugars, phosphates.

Amino Acids

Amino Acid Chains

Protein: Space Filling Model

α Helix Secondary Structure

Hemoglobin Protein Structure

Protein Functions

- Antibodies.
 - Recognize molecules of invading organisms.
- Receptors.
 - Part of the cell membrane; recognize other proteins, or chemicals, and inform the cell.
- Enzymes
 - Assemble or digest.
- Neurotransmitters, hormones
 - Trigger receptors.
- Channels and pores.

Cellular Absorption

- Diffusion.
 - Requires concentration gradient.
 - Fick's Law.
- Facilitated diffusion.
 - Membrane surface carrier proteins.
 - Glucose transport.
- Active transport.
 - Requires cellular energy (ATP).
 - Endo/exo-cytosis.
 - Phago/pino-cytosis.

Cell Membrane

Phospholipid bilayer

Four Types of Cells

- Epithelia.
 - Coverings, linings, secretions.
- Connective.
 - Support, energy.
- Muscle.
 - Movement.
- Nervous.
 - Electrical impulse, information.

Epithelia

Nerve

Eleven Organ Systems

- Integumentary
- Skeletal
- Muscular

- Nervous
- Endocrine
- Cardiovascular
- Lymphatic
- Digestive
- Respiratory
- Urinary
- Reproductive

Absorption

- Process by which toxicants cross the epithelial cell barrier.

Routes of Absorption

- Integumentary (percutaneous).
- Respiratory.
- Digestive.

Integumentary System Route

- Skin, hair, nails, mammary glands.
 - Skin is the largest organ in the body.
- Epidermis.
 - Avascular, keratinized stratum corneum, 15-20 cells thick, provides most toxicant protection.
- Dermis.
 - Highly vascularized; nerve endings, hair follicles, sweat and oil glands.
- Hypodermis.
 - Connective and adipose tissue.

Skin

Case Study: Skin Lesion

Respiratory System Route

- Skin: stratified squamous epithelial tissue.
- Respiratory system: squamous epithelium, ciliated columnar and cuboidal epithelium.
 - Non-keratinized, but ciliated tissues and mucus-secreting cells provide “mucociliary escalator”.
- Nasopharyngeal.
- Tracheobronchial.
- Pulmonary.

Respiratory Tract Respiratory System Route, 2

- Nasopharyngeal.
 - Nostrils, nasopharynx, oropharynx, laryngopharynx.
 - Hairs and mucus; trap $>5\ \mu\text{m}$ particulates.
- Tracheobronchial.
 - Trachea, bronchi, bronchioles; ciliary action.
 - Luminal mucus traps 2-5 μm particulates and H_2O soluble aerosols and gases.
- Pulmonary
 - Alveoli - high surface area gas exchange with cardiovascular system.

Lung Dissection Bronchus-Bronchiole Dissection

Case Study: Fixed Obstructive Lung Disease in Workers at a Microwave Popcorn Factory

Missouri, 2000--2002

- In May 2000, an occupational medicine physician contacted the Missouri Department of Health and Senior Services (MoDHSS) to report eight cases of fixed obstructive lung disease in former workers of a microwave popcorn factory. Four of the patients were on lung transplant lists.
 - All eight had a respiratory illness resembling bronchiolitis obliterans (chronic scarring) with symptoms of cough and dyspnea on exertion, had worked at the same popcorn factory at some time during 1992--2000

Diacetyl Butter Flavor

- Industrial hygiene sampling conducted during the November 2000 survey detected approximately 100 VOCs in the plant air.
- Diacetyl, a ketone with butter-flavor characteristics, was measured as a marker for exposure to flavoring vapors. The geometric mean air concentration of diacetyl was 18 ppm in the room air where the mixing tank was located, 1.3 ppm in the microwave packaging area, and 0.02 ppm in other areas of the plant.
- Rates of obstructive abnormalities on spirometry increased with increasing cumulative exposure to airborne flavoring chemicals.

Digestive System Route

- Mouth, oral cavity, esophagus, stomach, small intestine, rectum, anus.
- Residence time can determine site of toxicant entry/injury.
 - Mouth (short); small intestine (long).
 - Absorption of toxicants can take place anywhere, but much of the tissue structure in the digestion system is specially designed for absorption.

Gastrointestinal Tract Digestive System Route, 2

- Tissue differentiation.
- Mucosa
 - Avascular, s. squamous or columnar epithelium.
 - In some regions villi and microvilli structure aids in absorption (high surface area).
- Submucosa
 - Blood, lymph system interface.
- Muscularis (movement).
- Serosa (casing).

Intestine

Small Intestine Mucosa

Case Study: *Jin Bu Huan* Toxicity in Children – Colorado 1993

- Traditional Chinese herbal products are widely available in the United States (\$1B market).
 - Not marketed as drugs.
- Jin Bu Huan is manufactured in China, and the stated ingredients are Polygla Chinensis L. alkaloid (30%) and starch (70%).
- Used as a pain reliever.
 - Known hepatotoxin.
 - Associated with acute and chronic hepatitis.

Jin Bu Huan Toxicity: Patient 1

- A 13-month old boy was lethargic and breathing abnormally when found by his mother approximately 20 minutes after he ingested approximately 60 Jin Bu Huan tablets. The child exhibited CNS depression and was responsive only to

painful stimuli. In the emergency department, he was lethargic, with hypotonia, and transient bradycardia.

- An extensive toxicologic screen was negative. He was treated with activated charcoal through an orogastric tube. He became more alert during the next 10 hours until his physical examination and mental status were completely normal. Follow-up indicated no permanent sequelae.

Jin Bu Huan Toxicity: Patient 2

- A 2 1/2-year-old girl was lethargic and breathing abnormally when found by her mother 30-60 minutes after she ingested approximately 17 Jin Bu Huan tablets. Paramedics found the child unresponsive with respiratory depression. An acute episode of bradycardia was successfully treated with atropine. Initial examination in the emergency department indicated miotic pupils, CNS depression, and a disconjugate gaze. The patient's respiratory rate diminished, requiring intubation within 20 minutes after arrival to the emergency department. During the next hour, the child's condition improved, and during an episode of vomiting, she extubated herself.
 - Gastrointestinal decontamination treatment included performing gastric lavage and administering activated charcoal and a cathartic. She remained intermittently lethargic with diffuse muscle weakness until approximately 8 hours following ingestion. Urine and serum toxicologic screens were negative for more than 30 substances. She was discharged the following day after a complete recovery. Follow-up indicated no permanent sequelae.

Jin Bu Huan Toxicity: Patient 3

- A 23-month old girl was lethargic when found by her parents within 1 hour after she ingested approximately 7 Jin Bu Huan tablets. The child was transported to an emergency department 1 1/4 hours following ingestion.
 - Gastrointestinal decontamination consisted of performing gastric lavage (resulting in recovery of pill fragments) and administering activated charcoal and a cathartic. She was observed in the emergency department until 5 hours following ingestion and was discharged. Follow-up indicated no permanent sequelae.

Jin Bu Huan Toxicity: L-THP Alkaloid

- The tablets were 36% concentrated weight-by-weight levo-tetrahydro-palmatine (L-THP)
 - L-THP is present in the plant genus *Stephania* but not in the genus *Polygala* -- the plant of origin indicated on the Jin Bu Huan product package insert.
 - Morphine-like properties.

- Each tablet contained 28.8 mg L-THP; no other plant alkaloids were present in tablets tested from multiple bottles of Jin Bu Huan.