NEGATIVE EFFECT OF TCDD ON SOME ANIMAL ORGANS

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Definition

TCDD (2,3,7,8-Tetrachlorodibenzo-p-dioxin) is a compound from the dioxin Family, and it is considered one of the most toxic substances in this family

TCDD Belongs to a group of chemicals known as persistent organic pollutants (POPs)

Chemical Structure and Properties of TCDD

Molecular Formula: $C_{12}H_4Cl_4O_2$

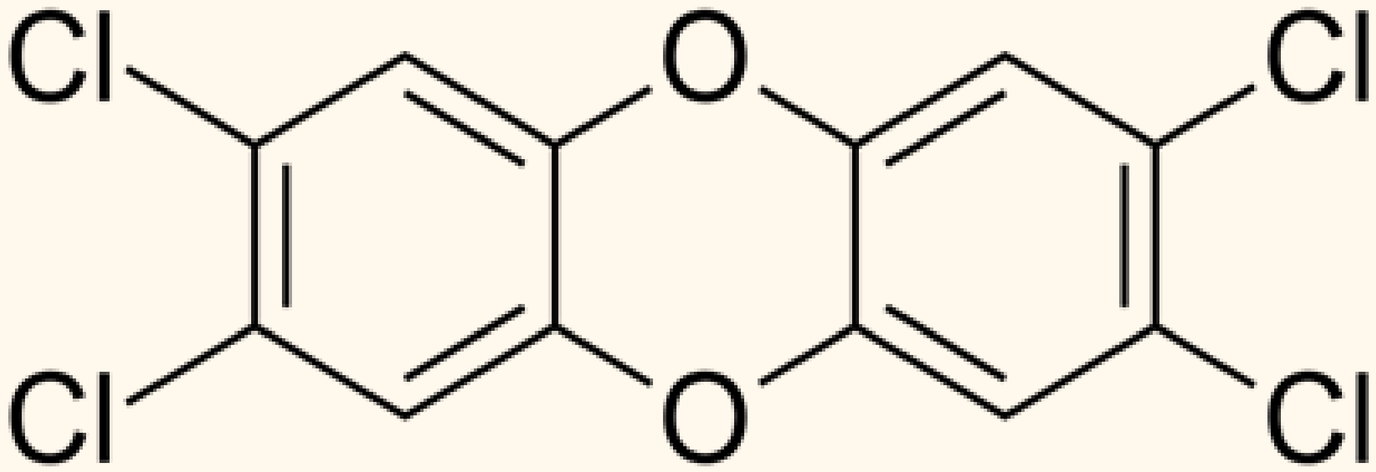
IUPAC Name: 2,3,7,8-Tetrachlorodibenzo-p-dioxin

Lipophilicity: TCDD is highly soluble in lipids (fats) but poorly soluble in Water

Stability: Due to its stable chemical structure, TCDD is resistant to Biodegradation and photodegradation;It is also .thermally stable and can withstand High temperatures

Low Volatility: TCDD has low volatility, which means it does not easily Evaporate into the air

Chemical Structure of TCDD



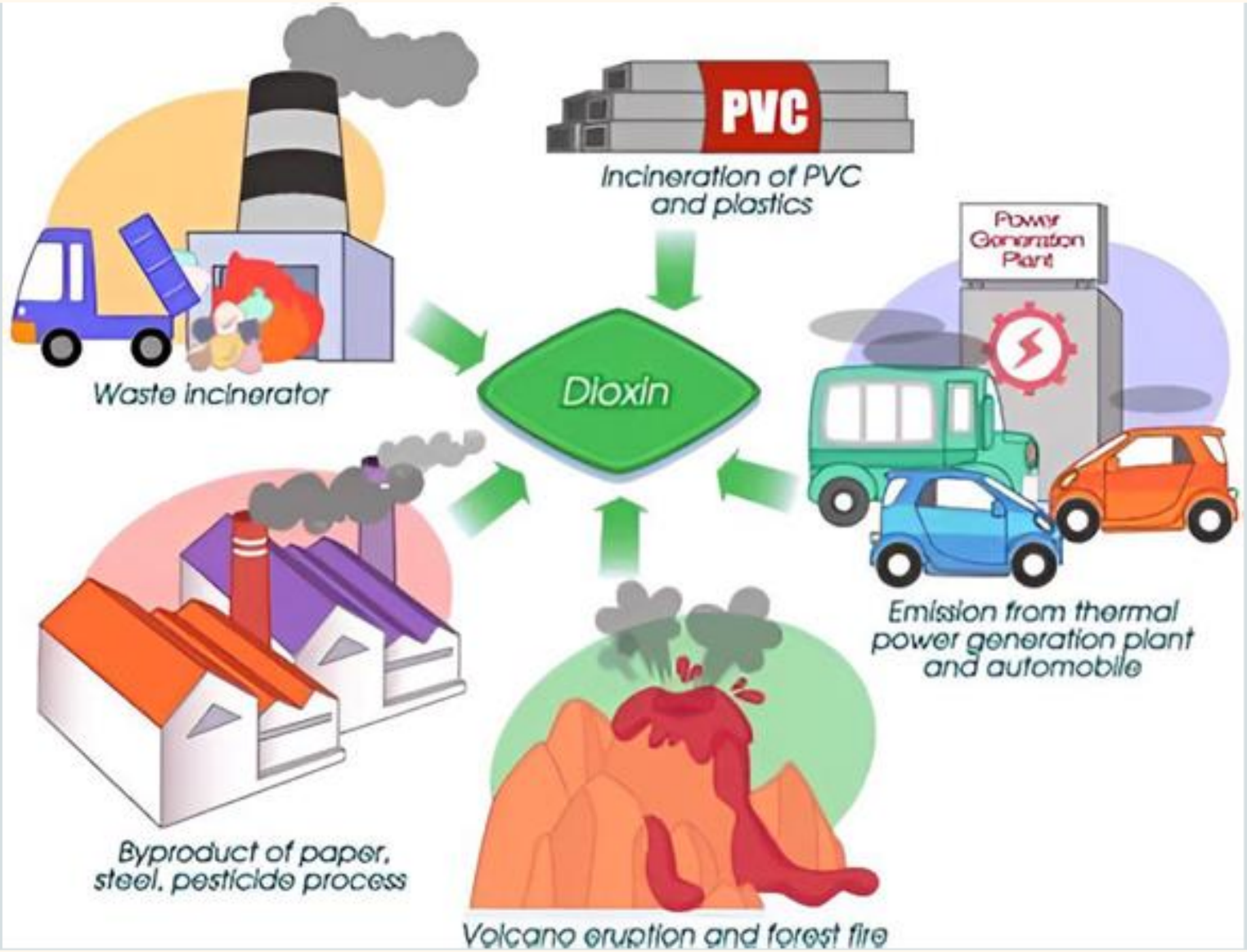
Sources of TCDD

TCDD is not produced intentionally but is a byproduct of various industrial And chemical processes:

Incineration and Combustion: TCDD is generated during the combustion Of organic materials Chemical Manufacturing: TCDD is a contaminant produced in the Manufacture of herbicides and pesticides (such as Agent Orange)

Industrial Processes: In industries like chlorine bleaching in the paper Industry and the production of certain chemicals

Natural Sources:wildfires and other natural processes can contribute to its release into the Environment


PVC
Incineration of PVC and plastics
Waste incinerator
Dioxin
Power Generation Plant
Emission from thermal power generation plant and automobile
Byproduct of paper, steel, pesticide process
Volcano eruption and forest fire

Methods of TCDD Exposure

Inhalation (Airborne Exposure):

- **Industrial Emissions: TCDD is released into the air as a byproduct of Combustion processes such as waste incineration, chemical manufacturing, and certain industrial activities**
- **Forest Fires or Open Burning: Burning certain materials like plastics or Chlorinated substances can release dioxins into the air**

Ingestion (Food Chain Contamination):

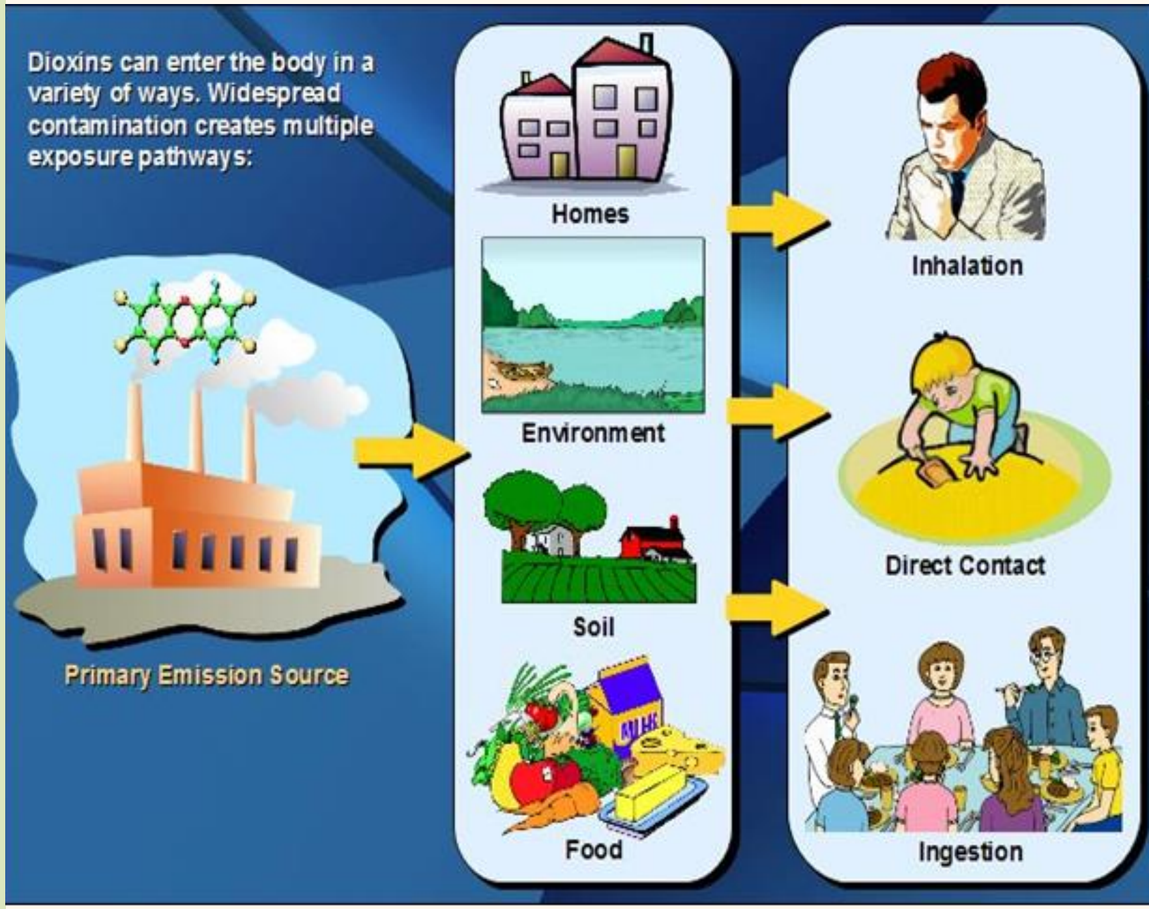
- **Contaminated Food:Dioxins bioaccumulate in the food chain, with higher Concentrations found in animal fat**
- **Drinking Water: contamination occurs due to industrial activities or waste disposal**

Methods of TCDD Exposure

Dermal Exposure

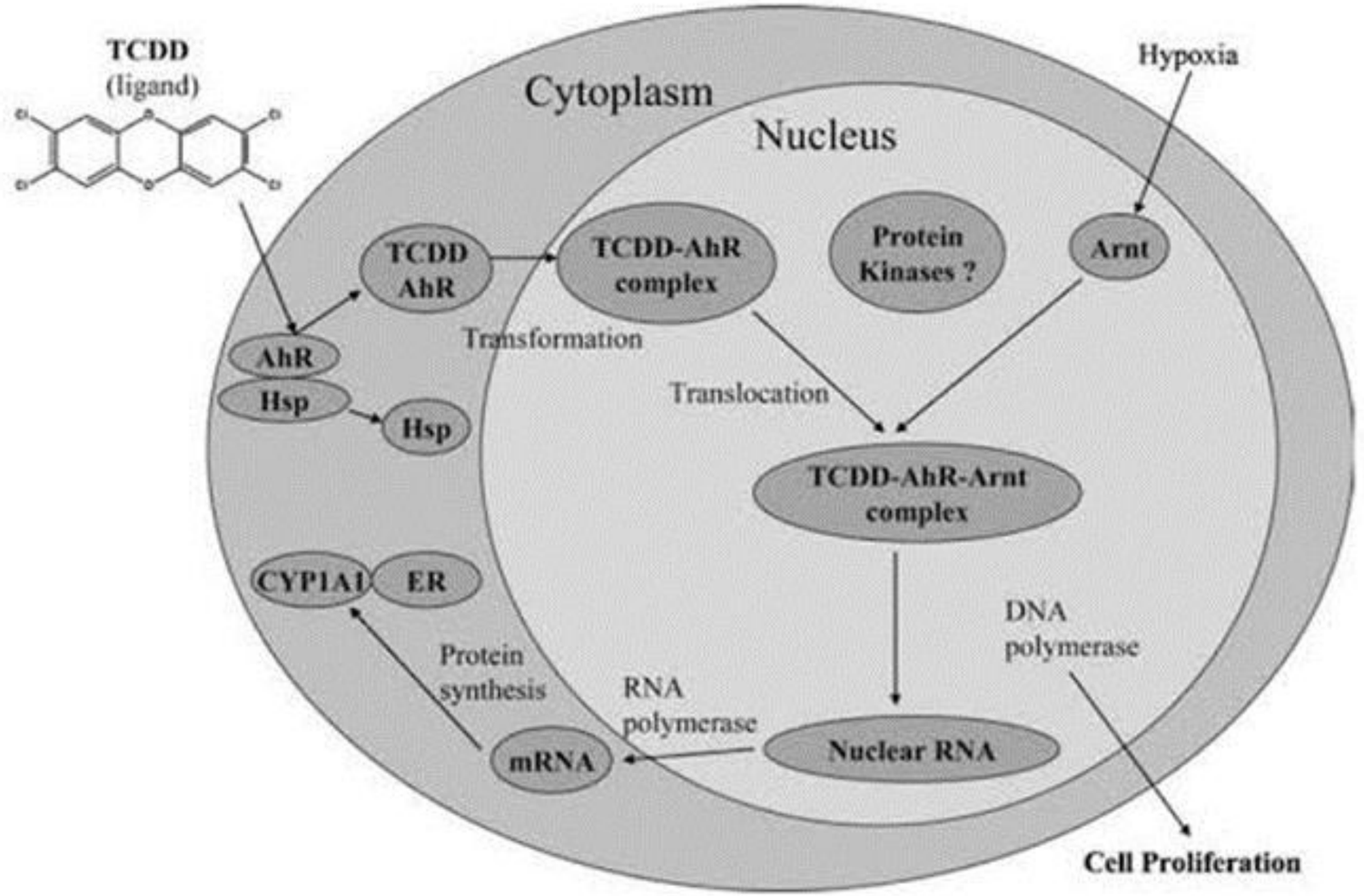
Soil and Dust Contamination: Direct skin · contact with contaminated soil or Dust can lead to dermal absorption of TCDD

Occupational Exposure: Workers in certain · industries (e.g., chemical Production) may experience dermal exposure to TCDD



Mechanisms of Toxicity

Fig. 3 Simple mechanistic model for TCDD toxicity using the AhR pathway. *ER* endoplasmic reticulum, *CYP1A1* cytochrome P450 1A1, *AhR* aryl hydrocarbon receptor, *Hsp* heat shock protein, *Arnt* Ah receptor nuclear translocator, *mRNA* messenger ribonucleic acid



Effects of TCDD on Human Health

Carcinogenicity: TCDD exposure is associated with an increased risk of Various cancers, including liver cancer, lung cancer, and soft tissue Sarcomas.

Reproductive and Developmental Toxicity:Birth defects;Reproductive · dysfunction, such as reduced fertility;Developmental delays

Endocrine Disruption:affecting thyroid hormones, sex hormones, and insulin signaling, leading to metabolic disorders and abnormal development

Neurotoxicity: leading to memory impairment, motor dysfunction, and learning difficulties

Immunosuppression: TCDD suppresses the immune system, increasing Susceptibility to infections and other immune-related diseases

Effect of TCDD on liver

Tumor Promotion:

TCDD promotes liver tumors by increasing altered hepatic foci (AHF), precursors to liver cancer.

Sensitivity varies among rat strains, with Long-Evans being more affected than Han/Wistar rat .

Hepatotoxicity:

Causes liver damage, indicated by elevated plasma liver enzymes .

Histopathological changes include necrosis, inflammation, fibrosis, bile duct hyperplasia, and cytoplasmic vacuolization.

Increased Liver Weight:

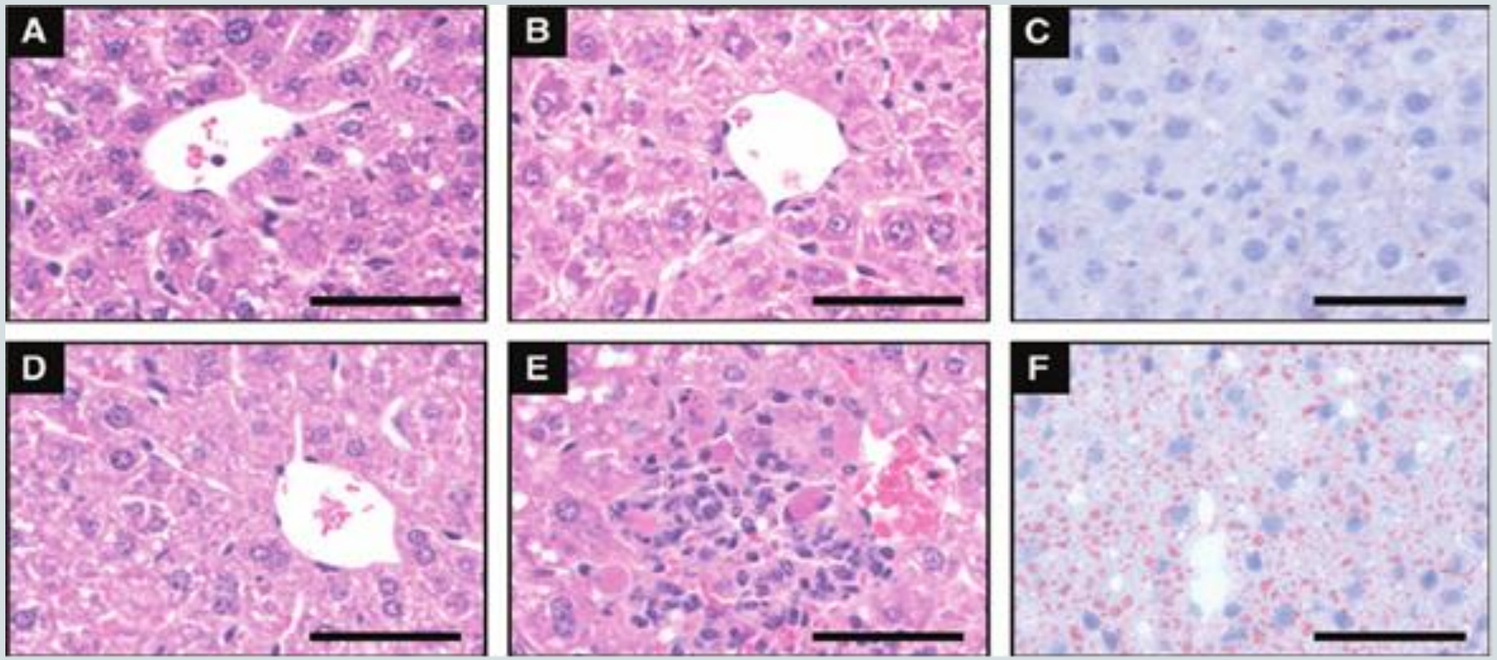
Leads to hepatomegaly due to hepatocyte hypertrophy and proliferation of the endoplasmic reticulum.

Often associated with reduced body fat.

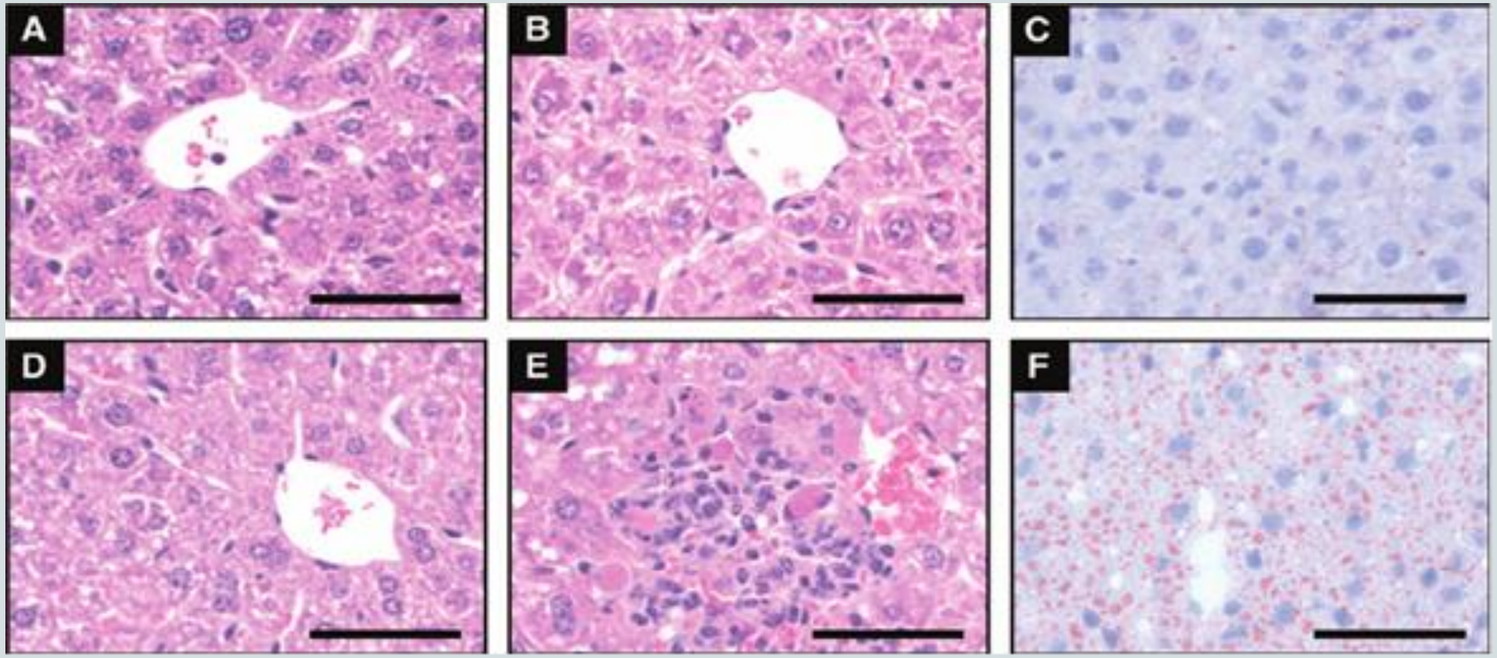
Oxidative Stress and Apoptosis:

Increases oxidative stress by elevating reactive oxygen species (ROS) and disrupting mitochondrial function.

Inhibits apoptosis, contributing to further liver cell damage and dysfunction.



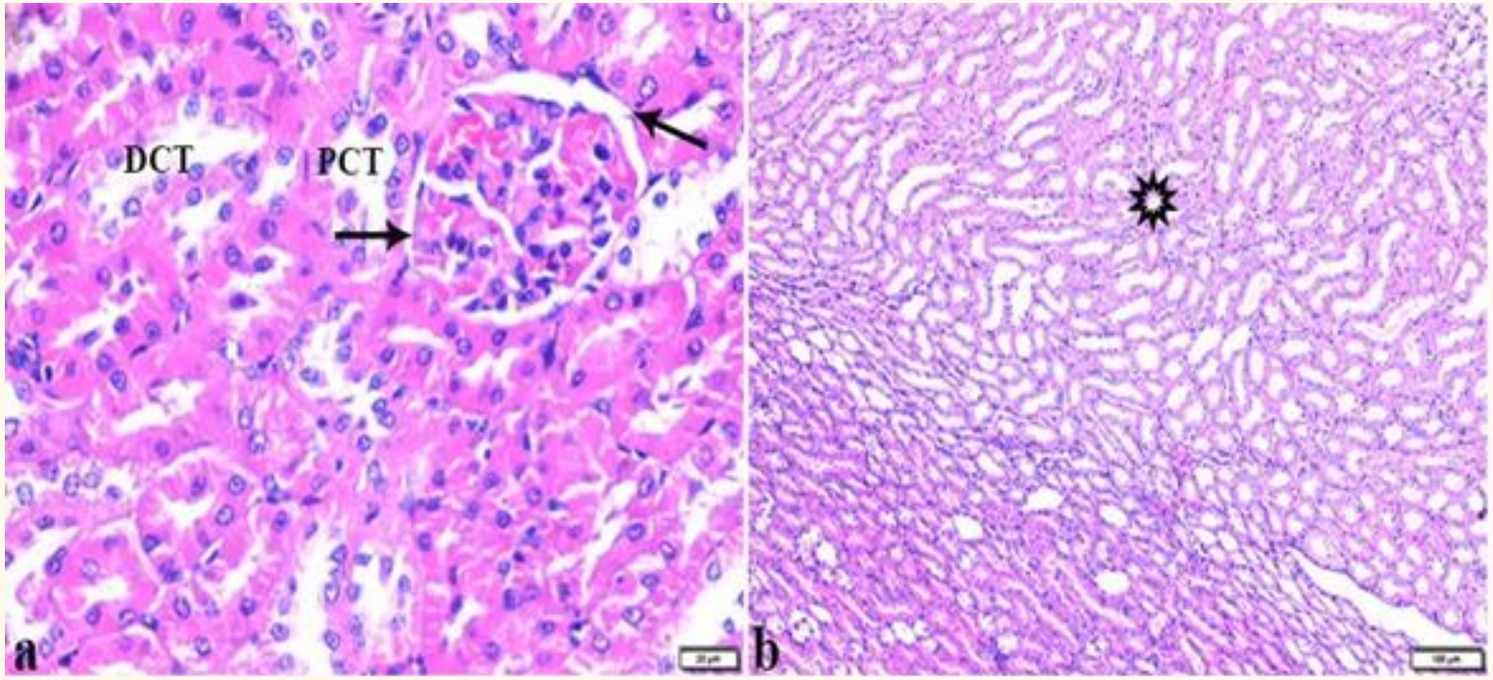
TCDD exposure in rats leads to minimal to moderate hepatocellular hypertrophy in the centriacinar liver regions 168 hours post-exposure. The affected hepatocytes exhibit more eosinophilic and less vacuolated cytoplasm compared to the centriacinar hepatocytes in control rats exposed only to the vehicle.



TCDD exposure in mice caused centriacinar inflammation, hepatocellular apoptosis, and periportal/midzonal lipidosis 168 hours post-exposure. Lipid accumulation in mouse livers was confirmed by Oil Red O staining, which was absent in rats. Comparable liver histopathology was observed in male rats treated with 40 µg/kg TCDD.

Effect of TCDD on kidney

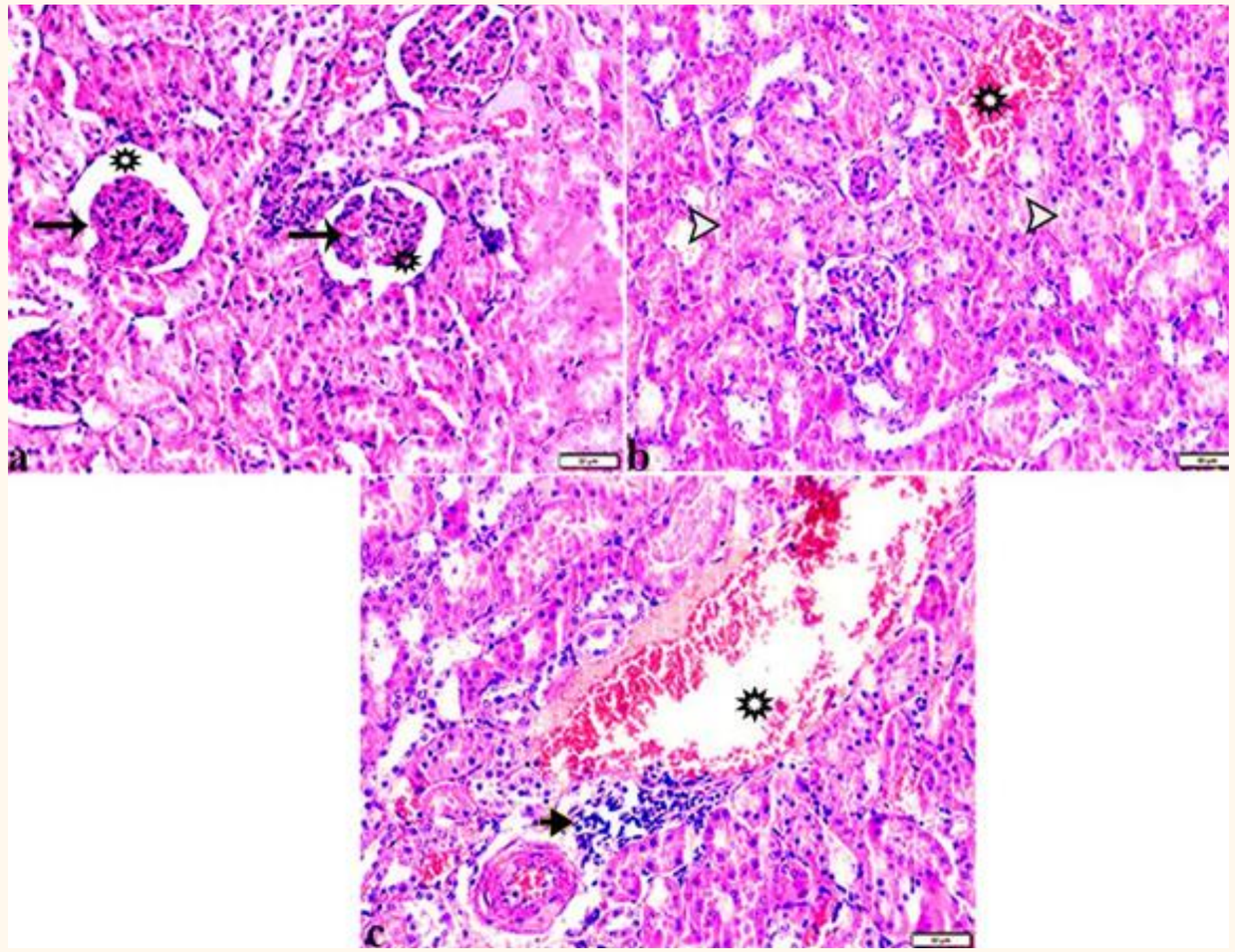
- Oxidative Stress and Cellular Damage:
- Induces oxidative stress, causing lipid peroxidation, protein oxidation, and DNA damage, disrupting renal cell function.
- Histopathological Changes:
- Leads to tubular atrophy, glomerular damage, and interstitial fibrosis with chronic exposure.
- Inflammatory Response:
- Activates inflammatory pathways, increasing pro-inflammatory cytokines and contributing to renal injury.



Photomicrograph of renal cortical tissue section from control group showing: (a): normal glomerulus (arrows), normal proximal convoluted tubules (PCT), normal distal convoluted tubules (DCT).
(b): normal renal medullary structure (star).
HE stains. The bar size is (a=20µm, b=100µm).

Photomicrographs of renal cortical tissue from the TCDD group reveal:

- (a) Glomerular tuft atrophy (arrows) and widened Bowman's space (stars).
- (b) Congestion of intertubular capillaries (star) and necrobiotic changes in renal tubular epithelium, including karyorrhexis and lysis (arrowheads).
- (c) Dilated and thrombosed arcuate vein with a thickened wall (star), accompanied by perivascular edema and mononuclear cell infiltration at the corticomedullary junction (arrow).
- Sections were stained with HE; bar size is 50 µm.



Effect of TCDD on Lung

Pulmonary Inflammation:

- Increases pulmonary inflammation, with immune cell infiltration (neutrophils, macrophages) and elevated inflammatory cytokines.

Impaired Lung Development:

- Disrupts normal lung development by interfering with signaling pathways involved in morphogenesis, leading to structural abnormalities.

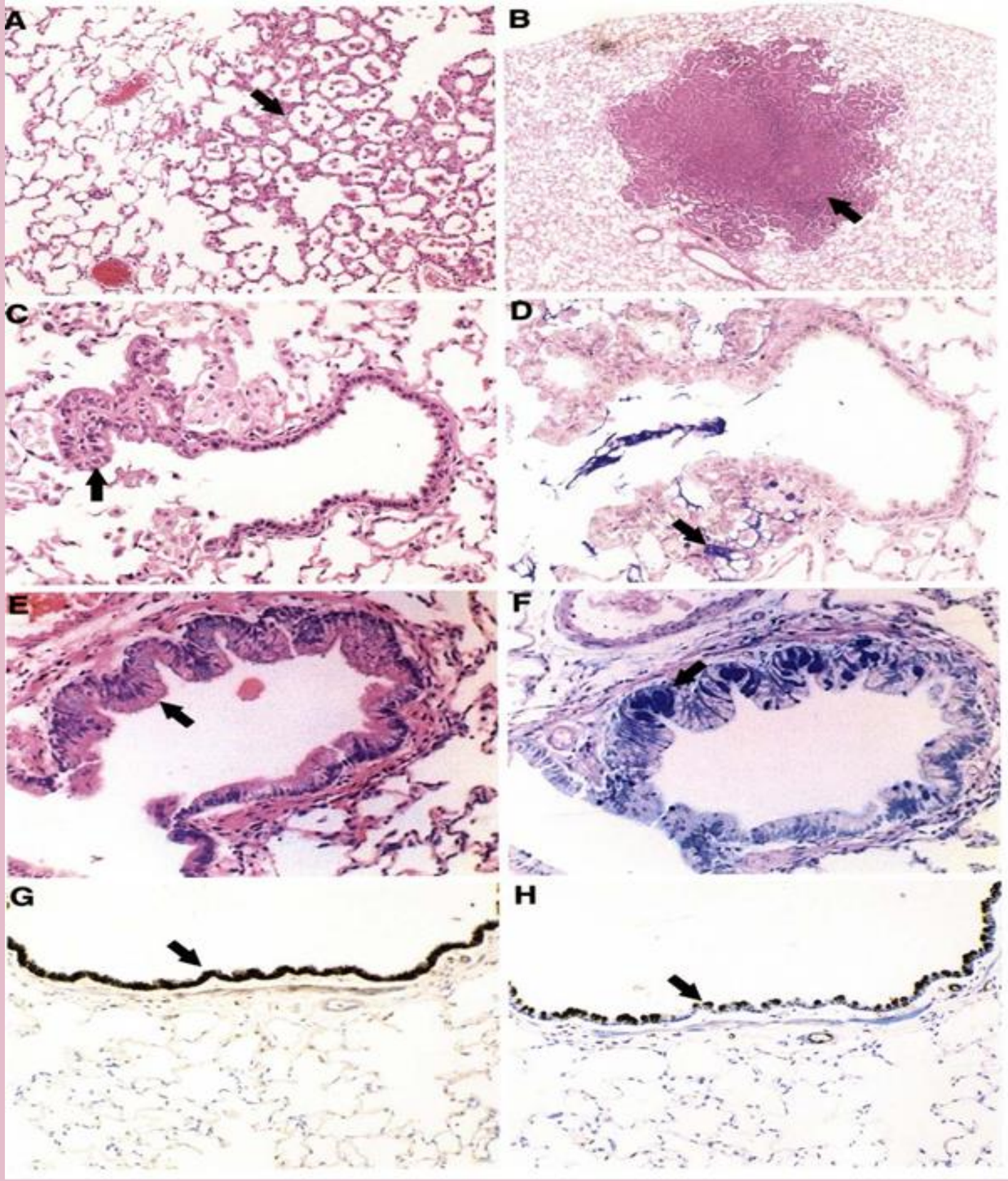
Oxidative Stress in Pulmonary Cells:

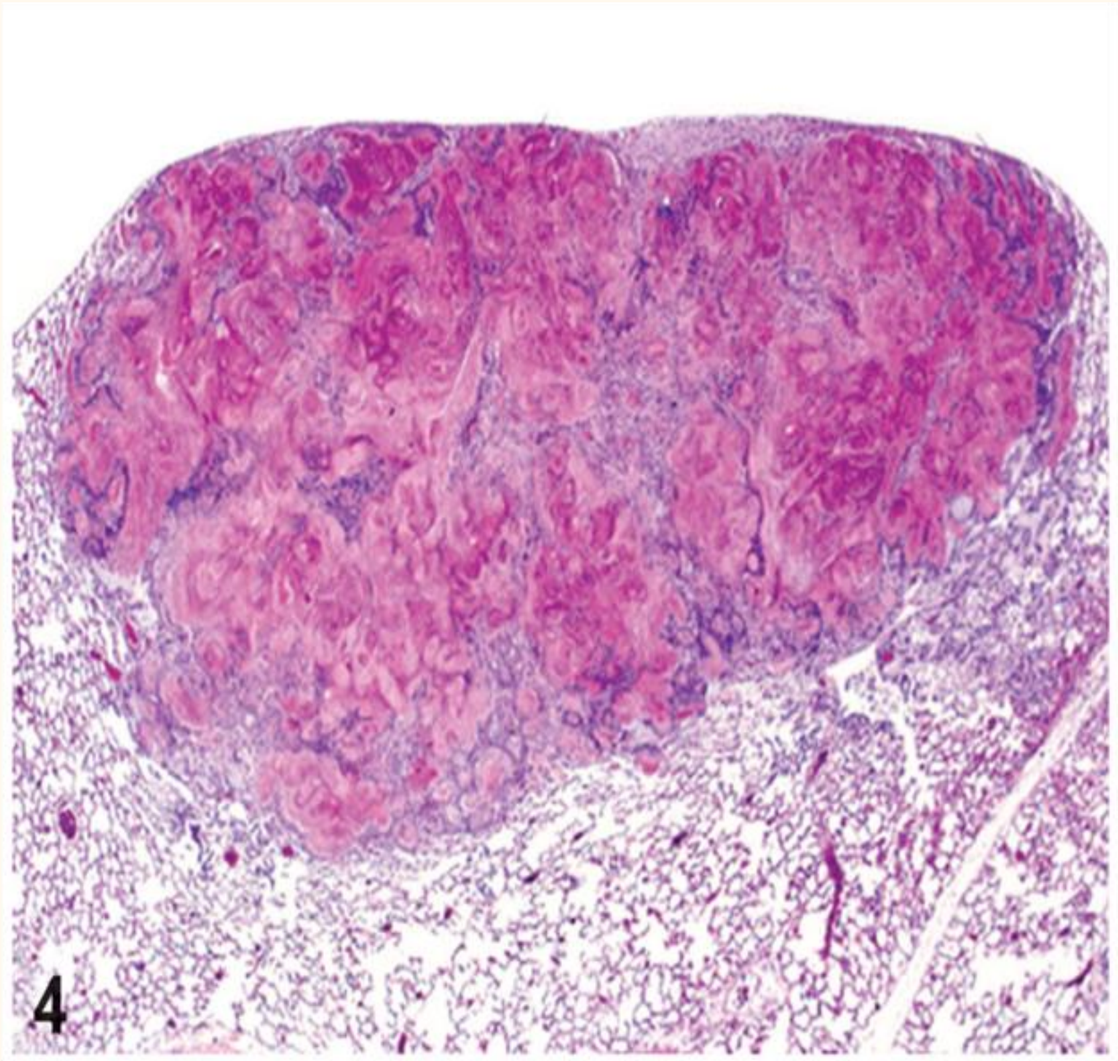
- Elevates reactive oxygen species (ROS) in lung tissue, causing oxidative stress and damage to DNA, proteins, and lipids.

Increased Risk of Lung Cancer:

- Long-term exposure to TCDD is classified as a human carcinogen, increasing lung cancer risk through DNA damage and chronic inflammation.

Magnifications for the photomicrographs are shown in parentheses. Lesions of concern and areas of specific protein expression are identified by black arrows (A) alveolar hyperplasia (X33); (B) AB adenoma (X 10); (C) AB metaplasia (X66); (D) AB metaplasia, Alcian blue stained for mucous substances (X66); (E) bronchiolar epithelial hyperplasia (X66); (F) bronchiolar epithelial hyperplasia, Alcian blue stained (X66); (G) AHR immunostain (X50); (H) CYP1A immunostain (X50).





Cystic keratinizing epithelioma. The mass is located in the lung below the thoracic serosa and has a center filled with keratin. TCDD study, H&E, X5.

فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ ۗ وَلَا تَعْجَلْ بِالْقُرْآنِ مِن قَبْلِ أَن يُقْضَىٰ إِلَيْكَ وَحْيُهُ ۖ وَقُل رَّبِّ زِدْنِي عِلْمًا

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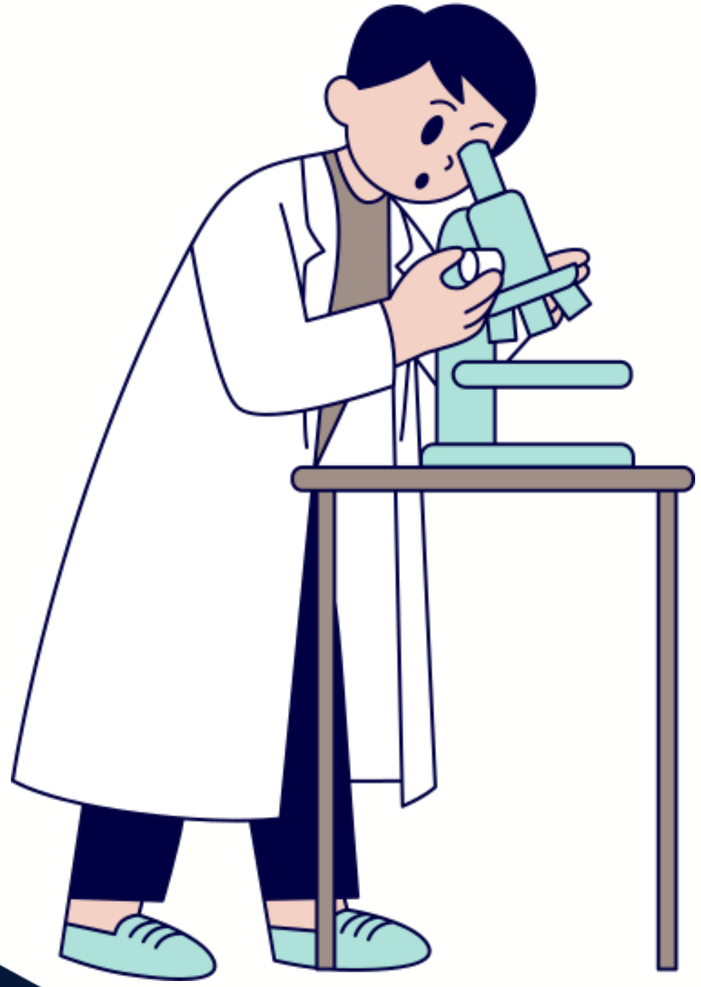

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