

## Pathological effect of Daily Consumption of Indomy on Lung, Kidney and Spleen in Albino Rat

Sura Fouad AL-Saffar<sup>1</sup>, Nusaibah Amer<sup>2</sup> and Amjed Torki Al-rudaini

Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq

<sup>1</sup>[sura\\_alsaffar@yahoo.com](mailto:sura_alsaffar@yahoo.com), <sup>2</sup>[nusaiba\\_hiso@yahoo.com](mailto:nusaiba_hiso@yahoo.com)

### Summary

This study aimed to investigate the histopathological changes of Indomy pasta for 30 days on lung, kidney and spleen of albino rats. fifteen adult albino rats 200-220 gm was divided into 3 groups: The first group was considered as control group. The second group was fed with Indomy every other day for 30 days; the third group was fed with Indomy every day for 30 days. The histopathological examination of the kidney show congestion of blood vessels and infiltration with neutrophil in lumen, The histopathological examination of lung showed hyper atrophy of musculares layer of the bronchiole with sever inflammatory cell infiltration mainly neutrophil and mononuclear cell in the wall of bronchioles, and with lumen of the alveoli with fibrous connective tissue proliferation in the parenchyma. Also, increase thickness into intra alveolar septa due to paranchymal cell proliferation and mononuclear cell infiltration which lead to narrow alveolar lumen. The histopathological examination of spleen shows congestion of the red pulp. From the results of this study it can be conclude that the consumption of Indomy had harmful histopathological effects on kidney, lung and spleen tissues in treated rats.

### دراسة مرضية لتأثير الاندومي في نسيج الرئة والكلية والطحال في الجرذان البيض.

سرى فؤاد الصفار و نسبية عامر احمد و امجد تركي الرديني

قسم علوم الحياة , كلية العلوم , جامعة بغداد

### الخلاصة

هدفت الدراسة الحالية الى التحري عن تأثير الاندومي على التركيب النسيجي للرئة والكلية والطحال في الجرذان البيض. وقد استخدم لهذا الغرض خمس عشر جرذا تراوحت اوزانهم 200-220 غم وقسمت إلى 3 مجاميع: المجموعة الأولى عدت مجموعة سيطرة. والمجموعة الثانية غذيت بالاندومي بين يوم وآخر لمدة 30 يوم، اما المجموعة الثالثة غذيت بالاندومي يوميا لمدة 30 يوم. بينت نتائج الفحص النسيجي للكلية احتقان في الأوعية الدموية واحتواء تجاويها على العدلات ، أما الفحص النسيجي للرئة فقد أظهر زيادة سمك الطبقة العضلية للقصيبات وتجمع العدلات والخلايا وحيدة النواة في جدار القصبية، فضلا عن حدوث تليفات في النسيج الرئوي مع احتقان في اللب الأحمر للطحال . اظهرت نتائج هذه الدراسة أن الإستهلاك الزائد من Indomy يسبب تغيرات مرضية في انسجة الكلية، والطحال والرئة في الجرذان المعاملة.

### Introduction

The Indomy is widely used pasta product all over the world .This study was designed to study the histological changes of highly consumption of this product on Kidney, Lung and Spleen tissue. The product composed of Pasta and flavor substances, which added to food as Food Colors, Preservatives, Antioxidants, Sweeteners, Emulsifiers, Stabilizers, Thickeners and Gelling Agents or Flavor enhancers and anti-bacterial and antifungal(1) .

These substances contain Sodium Bicarbonate : had a long history of use in food stuff, feed and industrial processes .the bicarbonate ion is normal constituents of vertebrates as the principal extracellular buffer in blood and interstitial fluids .the excess of sodium and bicarbonate excreted in urine, therefore assumed the normal handling and use will not have any adverse effects(2) , while the consequences of accidental or excessive oral ingestion had been described as causative of stomach rupture due to gas development and may cause metabolic alkalosis (3,4) reported that LD50 of oral administration in rats was 4,000 mg/Kg BW.

Potassium carbonate is odorless powder had slight toxicity by ingestion and severely irritant to body tissue and oral LD50 is 1870 Mg/Kg BW for rats (5).

Other components were Sodium phosphates: were added to many foods as an emulsifier to prevent oil separation like processed cheeses, processed meat, and readymade meal and tinned (canned) soups adding to food increase self life, maintaining texture and appearance of food (6).

Also Sodium phosphate is additive salt mainly used to keep PH stable or buffering NaCl and reduces microbial count (7),

Riboflavin (vitamin B2): is water soluble vitamin that helps the body to process amino acid and fat. It is antioxidant, but exposures to light destroy it (8).

Monosodium glutamate (E621): or glutamic acid is a chemical compound used in food as flavor enhancer .it had been classified by US Food and Drug Administration FDA as generally recognized as safe (GRAS) food additive( 9),The oral LD50 in rat is 1660 Mg /Kg BW (10).

The industrial food manufactures markets and use E621 as flavor enhancer because it balance blends and rounds the total perception of other taste (11).

While other study (12) reported some symptoms after taking of MSG and called it Chinese Restaurant Syndrome. Also (13) considered these symptoms as allergy in sensitive individuals. Other observation by (14) mentioned that the glutamate important neurotransmitters in human brain playing key element in learning and memory and excess glutamate can become neurotoxic.

## **Materials and Methods**

Experimental animals: 15 female albino rats, 3-4 months old and 200-220 gm body weight were housed in cages and maintained under laboratory controlled of temperature (25±2) , pelleted food and tap water were given.

Experimental design: Indomy was purchased from the local market in Baghdad. The animals were divided into three groups each of 5 rats. The first group (G1) was considered as control group. The second group (G2) was fed with Indomy every other day for 30 days; the third group (G3) was fed with Indomy every day for 30 days.

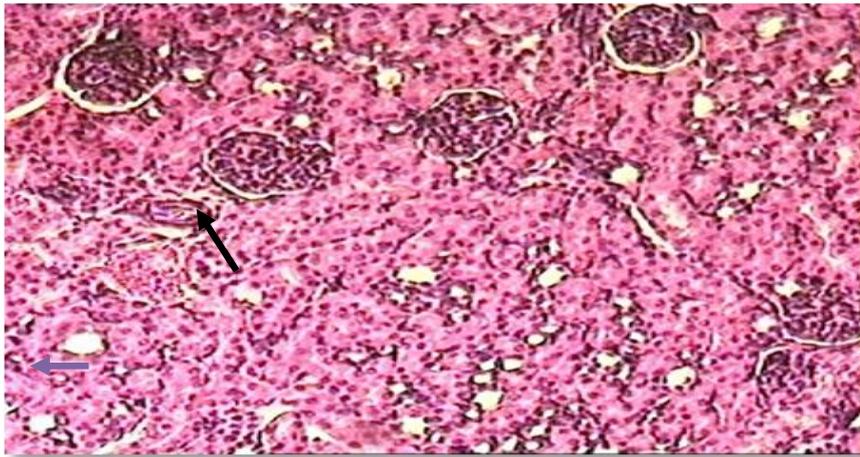
Histological examination: Animals were killed and specimens of Kidney, Lung and spleen tissues were taken from experimental animals were fixed in 10% neutral formalin, after 72 hr of fixation were processing with alcohol , paraffin-embedded and the section to mean thickness of 4 µm all tissues were stained with Hematoxylin and Eosin (H&E) stains according to (15) and histopathological were observed under light microscope .

## **Results**

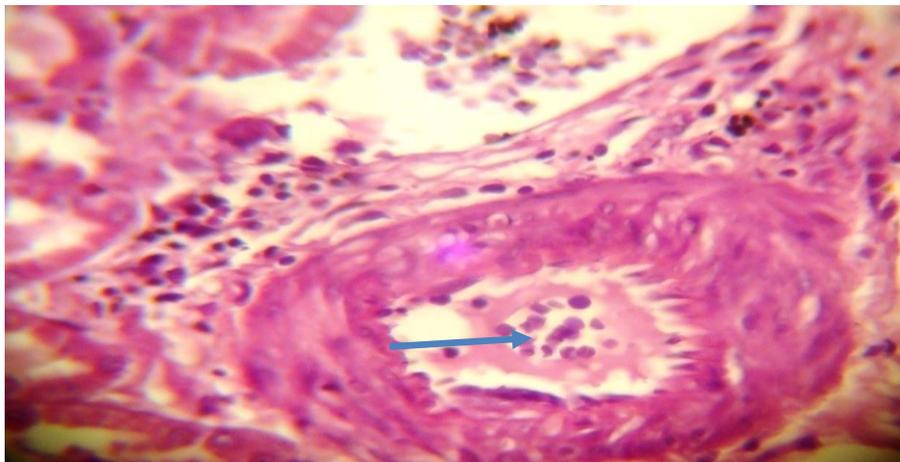
The Section of kidney tissue of control group showed normal Bowman's capsule, Normal convoluted tubules Figure(1), While, the histopathological examinations of the kidney of G2 showed congestion of blood vessels and infiltration with neutrophil in their lumen Figure. (2) while , Kidney of G3 revealed intense MNCs infiltration in the interstitial tissue figure (3). The lung tissue of control group (G1) shows normal alveoli and normal wall of alveoli Figure (4). While, the histopathological examination of lung G2 showed fibromascular hypertrophy of the bronchiole associated with sever inflammatory cell infiltration mainly neutrophil and mononuclear in the wall of bronchioles figure (5).

Also, increase thickness into intra alveolar septa of lung G3 due to alveolar cells proliferation and mononuclear cell infiltration which lead to narrow alveolar lumen Figure (6).

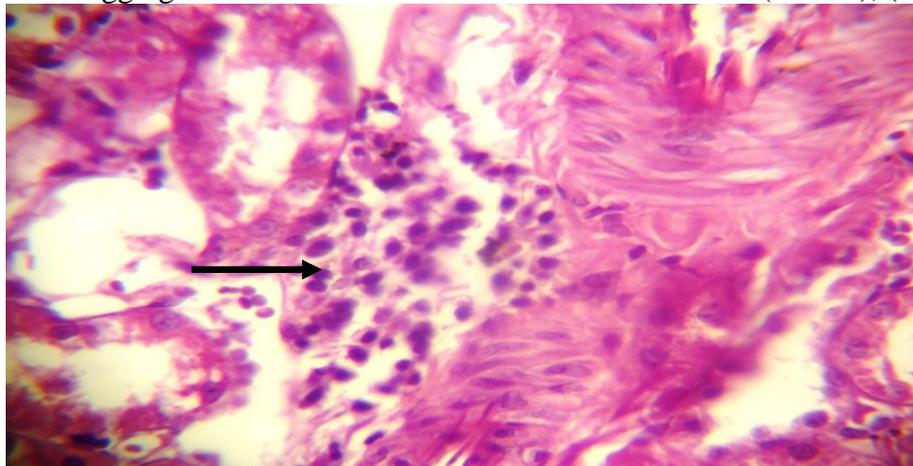
The Section of Spleen belongs to control group showed normal white pulp and normal red pulp Figure (7). While, the histopathological examination Of spleen G2 and G3 shows congestion of the red pulp with haemosedrin deposition Figure (8,9).



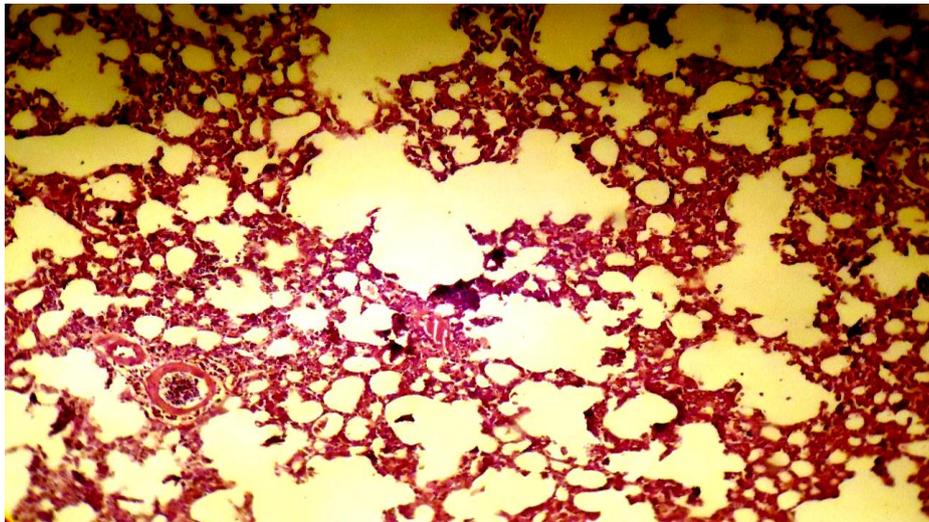
**Figure. (1):** Section of kidney tissue belongs to (G1) showed (  ) normal Bowman's capsule, and (  ) Normal convoluted tubules, (H&E) (100X)



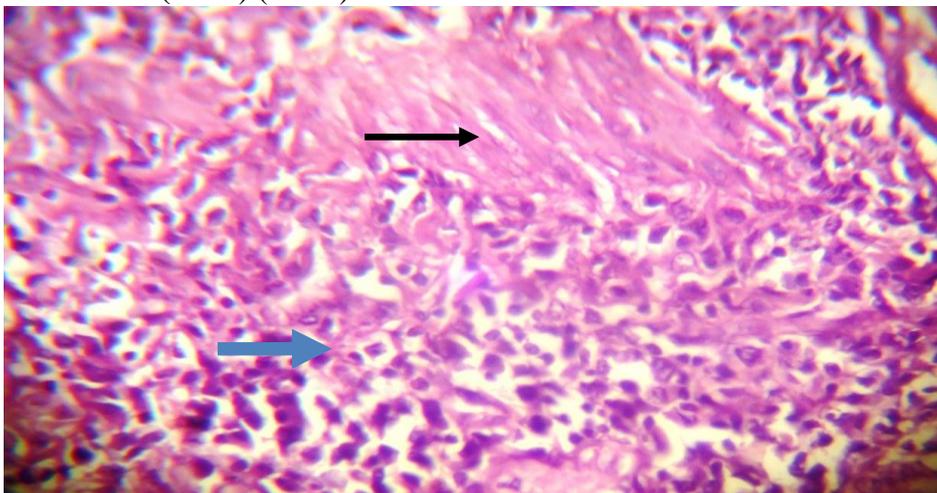
**Figure (2) :** Section of kidney tissue belongs to rat treated with Indomy (G2) showed mononuclear cell aggregation around blood vessel and in the lumen (  ), (H&E) 400X.



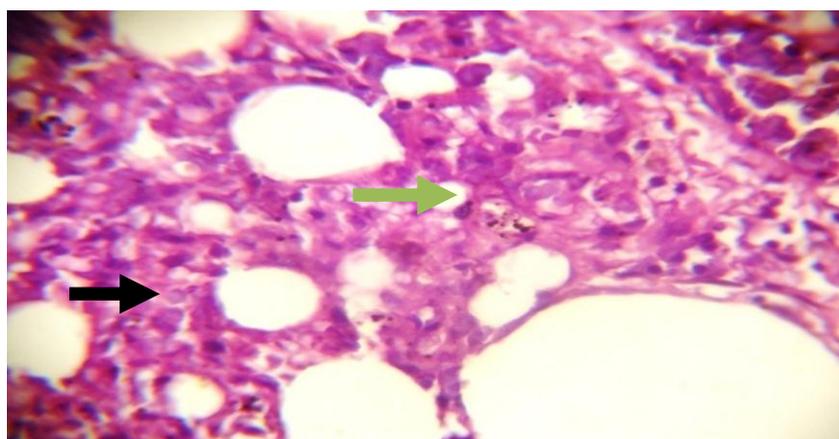
**Figure (3):** Section of kidney tissue belongs to rat treated with Indomy (G3) showed intense MNCs infiltration with neutrophil in the interstitial tissue (  ), (H&E) 400X.



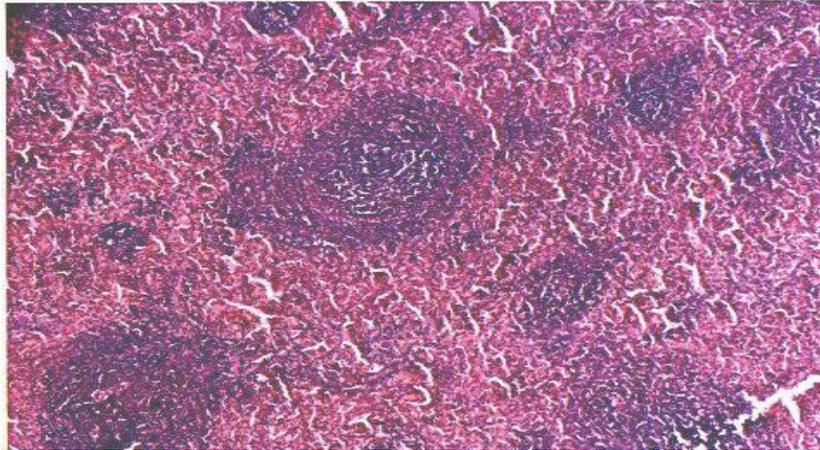
**Figure (4):** Section of lung tissue belongs to control group (G1) show normal alveoli and normal wall of alveoli (H&E) (100X).



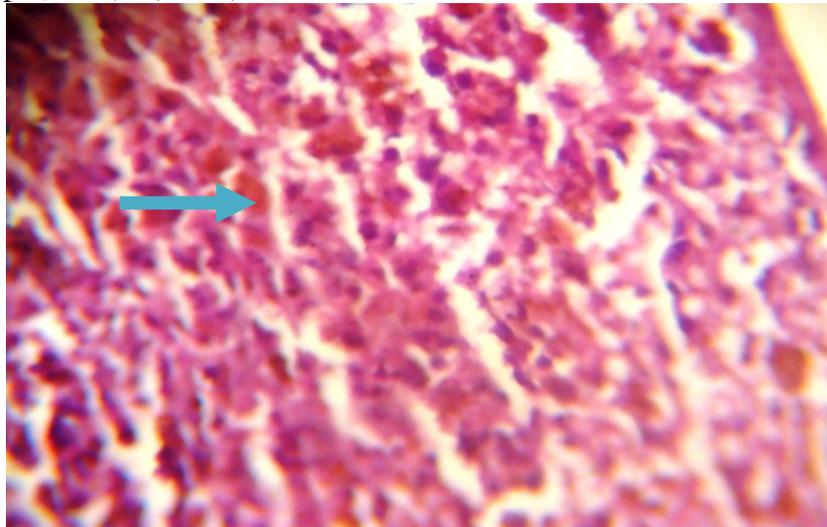
**Figure (5):** Section of lung tissue belongs to rat treated with Indomethacin (G2) showed fibromuscular hypertrophy of the bronchiole (black arrow) associated with severe inflammatory cell infiltration mainly neutrophil and mononuclear in the wall of bronchioles (blue arrow), (H&E) 400X.



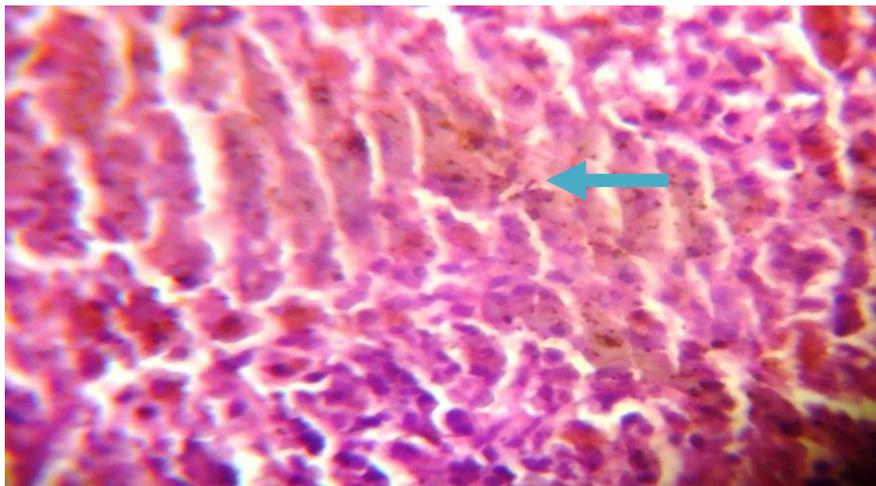
**Figure (6):** Section of lung tissue belongs to rat treated with Indomethacin (G3) showed increase thickness into intra alveolar septa due to alveolar cell proliferation (black arrow) and mononuclear cell infiltration which lead to narrow alveolar lumen. (green arrow) (H&E) 400X.



**Figure.7:** Section of spleen tissue belongs to control group showed normal white pulp and normal red pulp (H&E) , (100X).



**Figure (8):** Section of spleen tissue belongs to rat treated with Indomy (G2) showed Congestion of the red pulp ( →), (H&E) 400X.



**Figure (9):** Section of spleen tissue belongs to rat treated with Indomy (G3) showed Sever Congestion of the red pulp with haemosedrin deposition ( ←), (H&E) 400X.

### Discussion

The histopathological examinations of the kidney showed congestion of blood vessels and infiltration with neutrophil in lumen, These effects may be belong to sodium bicarbonate

which caused moderate to severe toxic effects. The most prevalent symptoms are excessive carbon dioxide production, metabolic alkalosis, cyanosis, hypernatraemia and diuresis (16). Although absorption of un neutralised  $\text{NaHCO}_3$  is known to cause alkalosis (2), this acid-base disturbance is usually transient in individuals with normal renal function, as the base excess will rapidly be excreted. The urinary pH can, however, be elevated by up to 1 unit, affecting tubular reabsorption and urinary elimination of weak acids and bases (2). The minimum dose causing adverse effects will vary strongly according to age and health condition, but for antacid use it is inadvisable to ingest more than 4 grams/dose (17).

Exposure to emulsion of potassium carbonate ( $\text{K}_2\text{CO}_3$ ) may participate with nephrotoxicity and induce liver damage. This also suggests a potential risk to humans who may come in contact with this supplement since liver and kidney are the major sites of chemical and drug metabolism(18), also sodium phosphate drug products had affected the renal function in adults by decrease glomerular filtration rate (GFR) (19).

Humans are exposed to dietary glutamate from two main sources – either from ingested dietary protein or ingestion of foods containing significant amounts of free glutamate (naturally present, or added in the form of MSG/hydrolyzed protein). Dietary glutamate is absorbed from the gut by an active transport system into mucosal cells where it is metabolized as a significant energy source. Very little dietary glutamate actually reaches the portal blood supply. The net effect of this is that plasma glutamate levels are only moderately affected by the ingestion of MSG and other dietary glutamates (20).

Also, the renal histopathological examination showed mononuclear cell aggregation around blood vessel and between renal tubules.

In a Stauffer's study (21), 5 male Sprague-Dawley rats per dose group were administered the test material (sodium tripolyphosphate, anhydrous) as 20% solution in water, at 464, 1000, 2150 and 4640 mg/kg, by gavage. The animals were observed for 14 days after treatment for mortalities and signs of toxicity.

No mortality occurred at the 3 lowest doses, and 2 animals died in the group treated at 4640 mg/kg. Clinical signs included acute depression, nasal discharge, dyspnea, and gasping. Gross pathological examination of the dead animals showed gross gastrointestinal haemorrhage, with congestion of the kidneys, adrenals, liver, lungs and heart.

While in other study, Histopathological examination showed tubular necrosis in the kidneys of rats treated at 10% sodium tripolyphosphate, and in the control group with 5% orthophosphate. Only inflammatory changes of the renal pelvis were observed at 2%, while normal kidneys were observed at 0.2%. Based on the renal effects, Furthermore, in this study, other groups of rats received similar doses of other inorganic condensed phosphates (sodium hexametaphosphate, sodium trimetaphosphate and sodium tetrametaphosphate), The effects on kidneys observed with STPP (Sodium Tripolyphosphate) in the two-year study were consistent with those reported in other less documented studies, and for various other inorganic condensed phosphates such as sodium hexametaphosphate, sodium trimetaphosphate and sodium tetrametaphosphate (22). They are possibly related to the phosphate and calcium imbalance in the organism which can result from high intakes of phosphorus.

In acute or chronic renal failure, the use of potassium-sparing diuretics and insufficient aldosterone secretion (hypoadosteronism) may result in the accumulation of excess potassium due to decreased urinary potassium excretion. This suggests that the emulsion of the carbonate might cause kidney damage. The significant decrease in protein synthesis as recorded in the study indicated possible damages to liver causing reducing protein synthesis. The rabbits treated with 100mg/L of the emulsion showed symptoms such as withdrawal from food, excessive thirst, drowsiness (weakness, reduced irritability, and polyuria, an indication of potassium acute toxicity (23,24).

The histopathological examination of lung showed fibro-muscular G2 hypertrophy of the bronchiole with sever inflammatory cell infiltration mainly neutrophil and mononuclear in the wall of bronchioles .

Also, increase thickness into intra alveolar septa of G3lung due to alveolar cells proliferation and mononuclear cell infiltration which lead to narrow alveolar lumen

The mononuclear cell infiltration which lead to narrow alveolar lumen that may refer to Indomy components like MSG which cause hypersensitivity pneumonitis (asthma attack characterized by bronchospasm and inflammation mucous membrane ) (25) , also sodium and potassium phosphate and considered as toxic salt they caused respiratory failure then death in mice ,rat and dogs (26) also the higher content of sodium bicarbonate in blood would cause pulmonary damage appeared as excess foamy macrophage ,and chronic ingestion there is pulmonary interstitial fibrosis(migrating ,activation and proliferation of fibroblast which induced by different factors like platelets ,inflammatory cells , injured epithelium an endothelium which stimulate fibroblast to secret extracellular matrix protein also it cause the yellow appearance of lung is due to bronchiolar obstruction refer to hypertrophy in bronchiole muscles as seen in lung section (27).

Increase of lipid peroxidation following MSG treatment (28) may be another factor that caused endothelial cell damage where the increase in lipid peroxidation leads to loss of membrane integrity, and cell degeneration (29).

This increase of neutrophils may be one of the possible mechanisms responsible for the present alveolar damage. And (30) reported that the neutrophils may injure lung tissue through either proteolytic enzymes (neutrophil intracellular granules contain elastase and collagenase, which can degrade and destroy lung alveolar cells) or reactive O<sub>2</sub> metabolite.

Lung section show sever inflammatory cell infiltration mainly neutrophil and mononuclear in the wall of bronchioles because the injured tissue act as strange body which stimulate the immune system and inflammatory cells to engulf the injured tissue and restore the normal tissue (31), the same effect were appeared in respiratory mucosa of rats were treated with potassium sorbate (32) , also (29) attributed the endothelial cell damage to the direct effect of the circulating toxins or to the release of vasoactive cytokines from macrophages and platelets or from the release of lysosomal enzymes.

The spleen sections of G2 and G3 showed congestion of the red pulp with haemosedrin deposition.

Data in animals are restricted to histopathological examinations of organs of the lymphoreticular system, but no information is available regarding possible effects on immunocompetence. Focal disintegration of cortical thymocytes was observed in rats especially Congestion of the red pulp.

Spleen Is only lymphatic tissue specialized to filter the blood this function is intimately related to its structure and particularly removes foreign materials, microorganisms and time expired erythrocyte and also remove inclusion bodies (residual DNA and denaturated hemoglobin), the toxic component increase the activity of spleen to remove it so that the red pulp appeared congested with highly deposition of hemosidrin (33) . Also sodium carbonate revealed spleen lesion in experimental to estimate the LD50 of it (34).

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