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UDC616:614:9:616
SRSTI 68.41.33
DOI: 10.52269/22266070_2023_2_9

HISTOLOGICAL AND ULTRASTRUCTURAL CHANGES IN CALF PARENCHYMAL ORGAN TISSUE AFTER ADMINISTRATION OF ISONIAZIDE

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The article highlights that young animals with TB were administered isoniazid (manufactured by McLeods Pharmaceuticals, India) as a means to promote alterations in the path morphology and ultrastructure of parenchymal organs in calves and guinea pigs, specifically the liver, lymph, and kidneys. These changes were examined using a modern electron microscope device, which encompassed both scanning and transmission microscopy techniques. The data obtained from various measurements (μm) were presented for analysis. For histological and ultrastructural investigations, a method involving the creation of hysteresis using epoxies resin.

Pathomorphological and ultrastructural changes encompass increased capillary permeability in lymph nodes, the presence of fat droplets with varying shapes and nuclear condensation of liver cells, diverse processes of dystrophy, and the appearance of fat droplets resembling "balls" in liver. Observed changes of the disintegration of nuclei within cells.

These studies allow for the determination of the extent of morphological and structural changes in the animals' bodies, assessment of the level of changes, confirmation of effectiveness, and the development of optimal therapeutic protocols, such as sequential medication.

Key words: Isoniazid; histological; ultra-structural; electron microscope; Isoniazid; calves; transmission; parenchymal organs.

ИЗОНИАЗИДТІ ҚАБЫЛДАҒАННАН КЕЙІН БҰЗАУЛАРДЫҢ ПАРЕНХИМАЛЫҚ МҮШЕЛЕРІНІҢ ТІНДЕРІНДЕГІ ГИСТОЛОГИЯЛЫҚ ЖӘНЕ УЛЬТРАҚҰРЫЛЫМДЫҚ ӨЗГЕРІСТЕР

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Мақалада туберкулез тіркелген шаруа қожалықтары төлін жұқпалы кеселден аман алып қалу мақсатында, изониазид (маклеоудс фармацевтикалс, Индия) дәрмегін беріп, оның бұзаулар мен теңіз шошқаларының паренхимиялық мүшелерінің (бауыр, лимфа түйіндері мен бүйректегі) патоморфологиясы мен ультрақұрылымындағы өзгерістеріне, қазіргі заманғы құрылғы электронды микроскоп (сканерлеуші және трансмиссионды электронды микроскоп) арқылы, түрлі (μm) ұлғайтқыштық өлшемдерде қарау арқылы алынған мәліметтер берілген. Гистологиялық және ультрақұрылымдық зерттеу үшін эпоксинді смола арқылы гисто кесінді жасау әдістемесі қолданылды. Гистологиялық зерттеу арқылы жануарлар ағзасындағы қайтымсыз түрлі патоморфологиялық, ультрақұрылымдық өзгерістер анықталды: лимфа түйіндерінің капиллярларының өткізгіштігінің күшеюі, бауыр жасушасында түрлі пішінді май тамшыларының кездесуі, бауыр жасушаларының ядролық конденсациясы, түрлі дистрофия үрдістері көрініс тауып, бауыр жасушаларында май тамшылары «шар» тәріздес көрінісі, эндоплазмалық тордың дөңестенуі, ядролары жасуша ішінде ыдырап, ядродағы тесіктер байқалды (май тамшыларының бауыр жасушаларына енуі салдарынан туындаған). Аталған зерттеулер арқылы, жануар ағзасындағы морфологиялық құрылымдық өзгерістер деңгейін анықтап, өзгерістер деңгейіне баға беріп, тиімділігін растауға, дәрмектердің дәйекті қабылдау секілді, оңтайлы емдік тағайындаулар жасауға мүмкіндік аламыз.

Түйінді сөздер: изониазид; гистологиялық; ультрақұрылымдық; электронды микроскоп; бұзау; трансмиссия; паренхималық органдар.

ГИСТОЛОГИЧЕСКИЕ И УЛЬТРАСТРУКТУРНЫЕ ИЗМЕНЕНИЯ В ТКАНЯХ ПАРЕНХИМАТОЗНЫХ ОРГАНОВ ТЕЛЯТ ПОСЛЕ ПРИЕМА ИЗОНИАЗИДА

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В статье описывается применение препарата изониазид (производство McLeods Pharmaceuticals, Индия) телятам не благополучных по туберкулезу хозяйств для сохранения здорового молодняка, а также определение его влияния в патоморфологию и ультраструктуру тканей паренхиматозных органов телят и морских свинок, в особенности печени, лимфатических узлов и почек. Эти изменения были исследованы с использованием современного прибора для электронной микроскопии, включающего сканирующую и трансмиссионную электронную микроскопию. В ходе исследования были полученны снимки в разных увеличениях (μm) для анализа. Для гистологических и ультраструктурных исследований, была использована техника создания гистосреза с использованием эпоксидной смолы. Гистологический осмотр выявил необратимые патоморфологические и ультраструктурные изменения в организме животных. Эти изменения включали повышенную проницаемость капилляров лимфатических узлов, наличие жировых капель различной формы, ядерную конденсацию клеток печени, разнообразные процессы дистрофии и образование жировых капель, похожих на "шары" в клетках печени. Другие наблюдаемые изменения включали выпячивание эндоплазматической сети, дезинтеграцию ядер внутри клеток и наличие пор в ядре (вызванные проникновением жировых капель в клетки печени). Эти исследования позволяют определить степень морфологических и структурных изменений в организме животных, оценить уровень изменений, подтвердить эффективность и разработать оптимальные терапевтические протоколы, такие как последовательное лекарственное лечение.

Ключевые слова: изониазид; гистологический; ультраструктурный; электронный микроскоп; теленок; трансмиссия; паренхиматозные органы.

Abstract

The problem of zoonotic tuberculosis continues to be a global concern, despite efforts to control the spread of the disease over the past 15 years. In countries with low economies, where tuberculosis is widespread, effective measures for controlling the transmission of Mycobacterium bovis, the causative agent of bovine tuberculosis, and for identifying the source of the human disease-causing agent, Mycobacterium

tuberculosis, are necessary. However, due to the difficulty in distinguishing Cattle TB bacillus from Human TB bacillus, exact information registered TB occurrences is often lacking [1, p.83; 2, p. 6; 3, p.89; 4, p. 16; 5, p. 77; 6, p. 52].

The risk of transmission is particularly high in areas where bovine tuberculosis is endemic and where people come into direct contact with infected animals (such as farmers, veterinarians, and butchers) or consume unpasteurized dairy products and other unprocessed animal products [7, p. 65].

The World Organization for Animal Health has recently emphasized the need for an integrated, multidisciplinary approach to prevent and control zoonotic tuberculosis, which involves considering the connections between humans, animals, and the environment. Bovine tuberculosis is a major animal disease that contributes to this public health concern [8, p.98].

The aim of this study is to investigate the pathomorphological, histological, and ultrastructural changes in the parenchymal organs of calves following treatment with isoniazid. By examining these changes, we hope to gain a deeper understanding of the effects of isoniazid on these tissues and their potential implications for the treatment of tuberculosis in animals and humans.

Materials and Strategies

Work accomplished at Zhangir Khan WKATU's laboratory, engaging animals from local farms, also morphological studies realized using the electron microscopes of the Kazakh-Japanese laboratory of KAZNARU, Kazan State Veterinary Academy (Russian Federation), the Scientific Center for Radioecological researches at Shakarim University, the Saratov National State University.

During the study, four calves and ten guinea pigs were used, and four heads of cattle were tested for allergic reactions. Four calves were specially slaughtered for path morphological, histological, and ultrastructural studies. Thorough measures against tuberculosis aimed at preventing the disease were implemented, and pharmaceutical substances were given to four livestock heads in a pair of agricultural farms.

Calves and laboratory animals divided in two groups, first group administrated first 30 days with Isoniazid drug, second group of animals were control group. All animals were negatively tested for allergy. Calves and Lab animals got *per os* isoniazid in 10 mg per 1 kg during the 30 days. After they were injected by BCG vaccine. Two animals from each group were examined for morphological changes after four and twelve months. Visceral organs and lymph nodes were picked up for examination.

Results

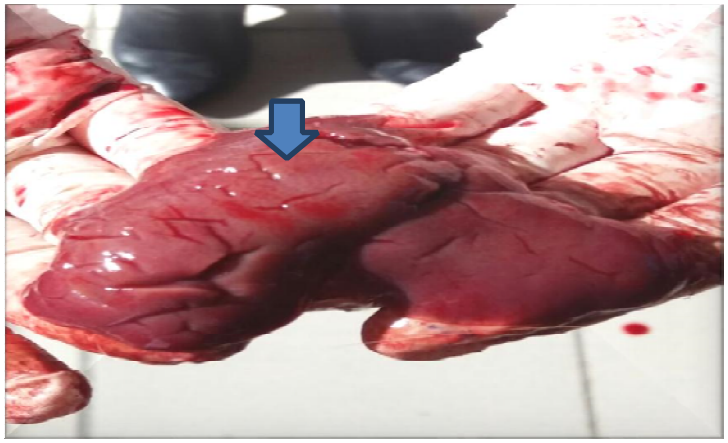
There were determined microscopic grains in liver tissues of lab animals (figure 1). The Vascular congestion, venous stasis, Perivascular hemorrhage was found around the dilated veins.

The number of hepatocytes with altered protein synthesis is consistently increased. In some areas, there is a localized buildup of histolytic cells within the tissue of the organ.

The lymphoid channels are enlarged, with immune cells inside them. The phenomenon of lymphoid cell proliferation is evident within the sinuses, especially in the form of impact cells and mitotic shapes.

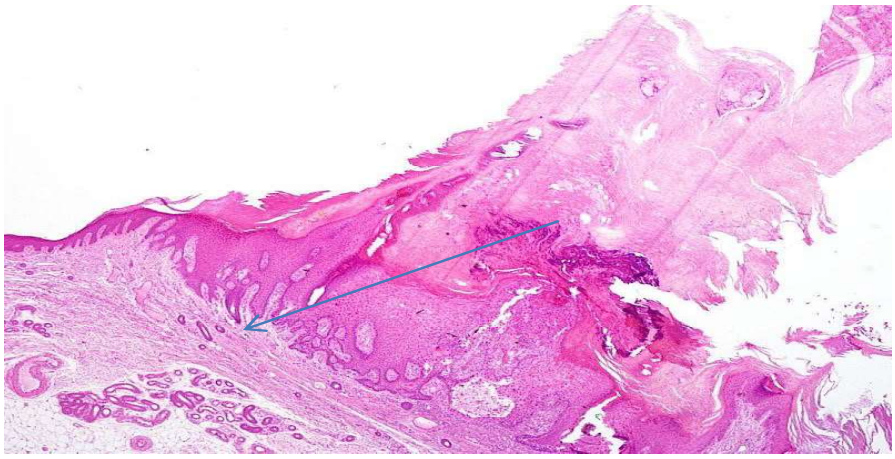
The sinuses' inner contained intricate Thrombin substrate networks, and there was a significant presence of Immunocytes. However, the Inner cortex region of the node had few intro cellular structures. Researchers observed a substantial influx of plasmocytes into the lymph nodes and Tarsal bone in young cattle.

The fibrous tissue of the lattice-like structures is distended; the cells are reduced within the intricate network of immune system centers. It has been observed that the tissue surrounding the blood vessels in the lattice-like structures is enlarged and engorged; white blood cells such as T cells and natural killer cells are penetrating it.

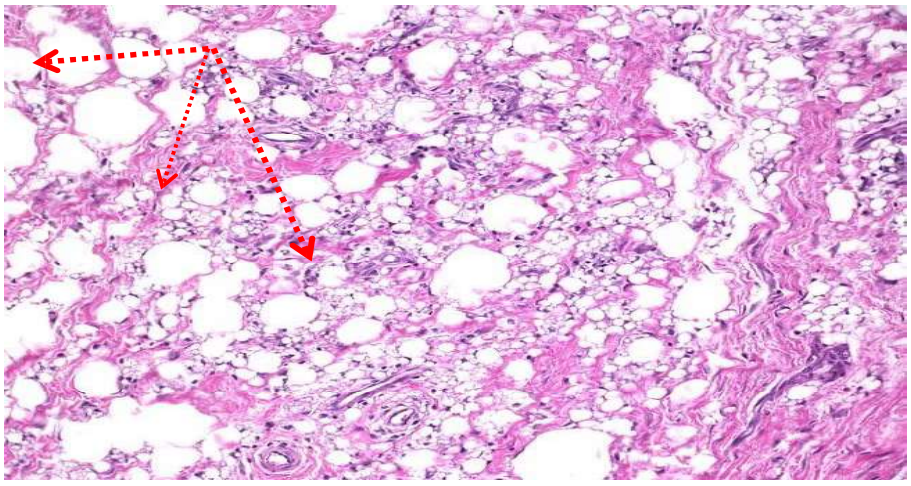


Figrure 1 – The hepatic steatosis of the guinea pigs liver and structural alterations within the liver.

There was a focal increase in thickness of the small air sac cells in the pulmonary organs as a result of filtration by lymphocytic cytotoxic cells.. In the liver and kidneys, stasis of blood flow Was noted inside the vasculature of the young bovines in the outer layer, lymphatic obstruction with the porosity of small hair-like vessels (illustrated in figure 2), grainy and oily degeneration of the functional tissues (shown in figure 3), and an increase in the number of tissue-resident immune cells and in some areas, signs of dead tissue were noted.



Figrure 2 – Hemostasis in blood vessels, appearance of lymph stasis in capillaries x 230



Figrure 3 – Hemostasis in blood vessels, appearance of lymph stasis in capillaries x 230

Therefore, noticeable histological modifications were noted in the hepatic and renal organs of animals, characterized by infiltration of hepatocytes and fat degeneration.

Submicroscopic changes in vital organs and tissues of animals administered with isoniazid were noted.

Upon examining the submicroscopic structure of vital organs following isoniazid administration, we observed alterations in liver and kidney cells.

With regards to this matter, we will focus on a specific area of calf organs exposed to isoniazid.

During histological examination of laboratory animals, indications of lipid deterioration were detected in the hepatic, renal, and cardiac tissues of the cavy.

After 15 days of observation in young cattle, we discovered that those liver cells, due to internal compensatory force, migrated towards the periphery of the nucleus. Additionally, swollen mitochondria and fatty deposits were identified (illustrated in figure 4).

Mitochondria in liver parenchymal cells exhibit various oval and circular shapes, with elongated filamentous shapes occasionally visible.

The endoplasmic reticulum is closely associated with mitochondria, appearing in a smooth and granular form. The Golgi complex layer situated at the core of the nucleus and bile ducts, resulting in the formation of Foam with a sleek facade. A dense material from these vesicles is distinguishable: lipids. Upon sectioning the parenchyma, a few dense bodies were observed. These compact Entities are Identical and Saturated. The fragile composition of the grains has been altered.

In the hepatic organs, following a period of 1 months, reduction in fibril, a shorten within the swelling of the endoplasmic mesh, tiny formed chondriosomes within the cell, smashed nuclei and openings within the nucleus. The quantity of chondriosomes amplified several times, the endoplasmic mesh was apparent, and the technique of nuclear division was acknowledged.

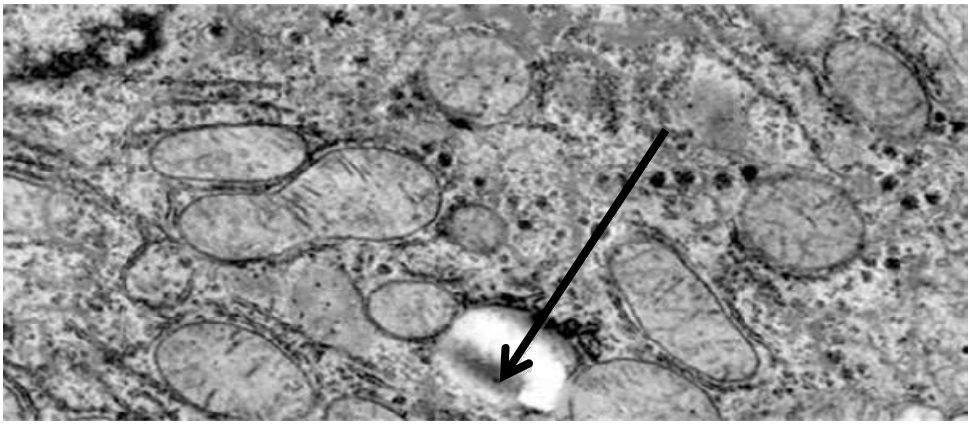


Figure 4 – Proximity of adipose globules within the liver, inflated chondriosomes.
alpha-ray magnifier observes (a,b,c,d) x 240; beta-various chondriosomes, lipochrome X 3200

Electron-opaque chondriosomes and fatty degeneration of liver and renal cells were identified (Figures 5, 6). The bilayers of renal cells' membranes consist of homogeneous diffusing chromatin. Albeit nuclei exist, detecting them can be strenuous. From electron micro-imagery, mitochondria from cellular cytoplasms, certain clusters of Golgi vacuoles, infinitesimal granules, and ribonucleoprotein granules were also apparent. The intercellular body amidst cellular nuclei is dense and fused without apparent crushing plates. Organic epithelial cells occupy the complete exterior of the inter-capillary cavity. In the cytoplasm of these cells, stretched out protrusions like trabeculae or peduncles (the foot handle) were discovered.

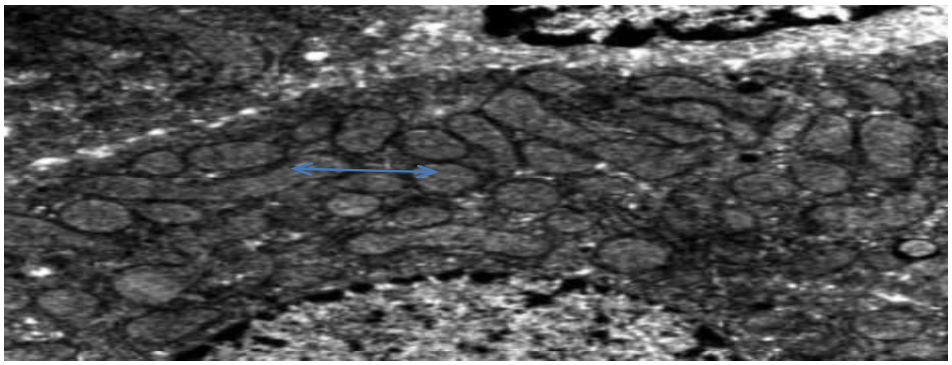


Figure 5 – Amplification in the quantity of chondriosomes in hepatocytes in the liver

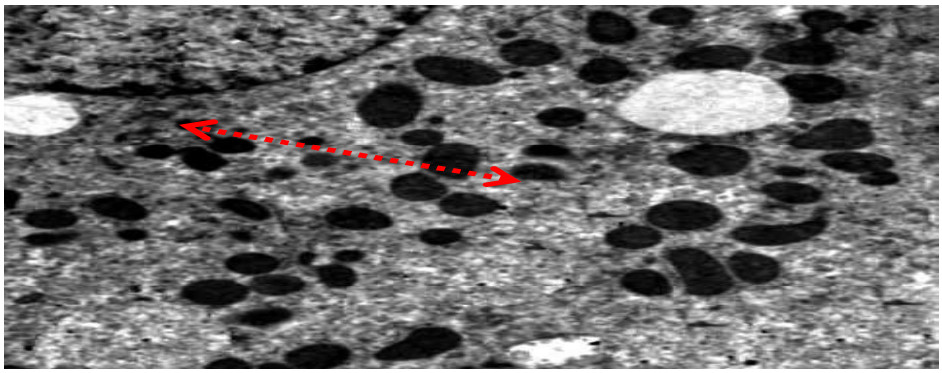


Figure 6 – Electron-dense chondriosomes in the renal organs X 30,000

The cytoplasm of bony spicules and the cellular body are uncomplicated. Even though the quantity of chondriosomes is small and large, the configurations of the vacuoles do not correspond to the standard shape. We have observed Golgi vacuoles in some regions. Within the epithelium, the cellular nuclei were

elliptical. Glycogen compounds were not identified after 320 days. Additionally, no alterations in cellular organelles were perceived after 30 days. However, indications of fatty degeneration were observed (figure 7).

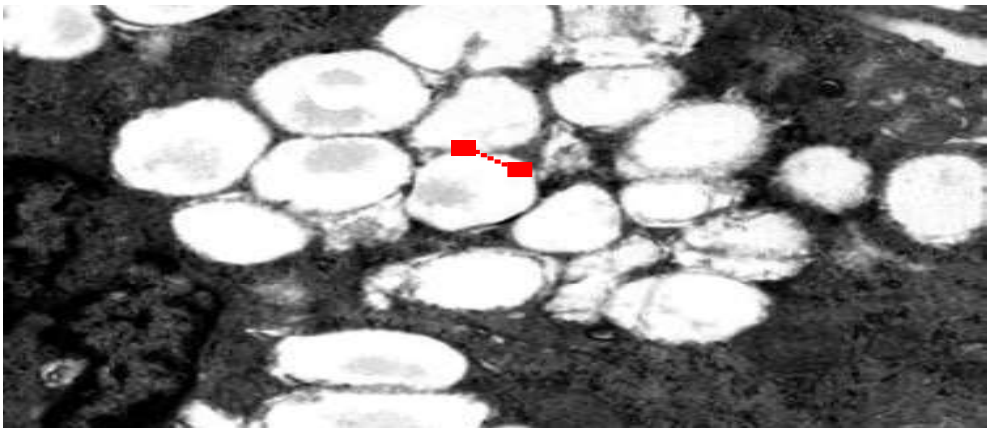


Figure 7- Fatty dystrophy hepatic organs

Upon observation through a filter magnifier, external entities with a gritty texture were discerned on the surface of liver tissues (figure 8). When utilizing isonicotinic acid hydrazide, as demonstrated by our analyses in the histological examination, domestic cavy specimens exhibit adipose of hepatic cells. After analysing the changes in structure, after two weeks, there were discovered that hepatic cells, due to internal compensatory pressure, relocated to the periphery of the nucleus. Moreover, enlarged mitochondria and lipid droplets appeared within an expanded bulge, and the lipid bar was conspicuous in some areas. In the liver, after 30 days, there was a reduction in hepatic cell microfiber, a decrease in endoplasmic reticulum bulging, diminutive mitochondria within the cell, obliterated nuclei, and lacunae within the nucleus. The cells of the liver exhibited notable increases in the number of mitochondria, nuclei, and endoplasmic reticulum. Additionally, there were signs of deterioration in the electron-dense mitochondria and the accumulation of fatty deposits in the cells of both the liver and kidneys.

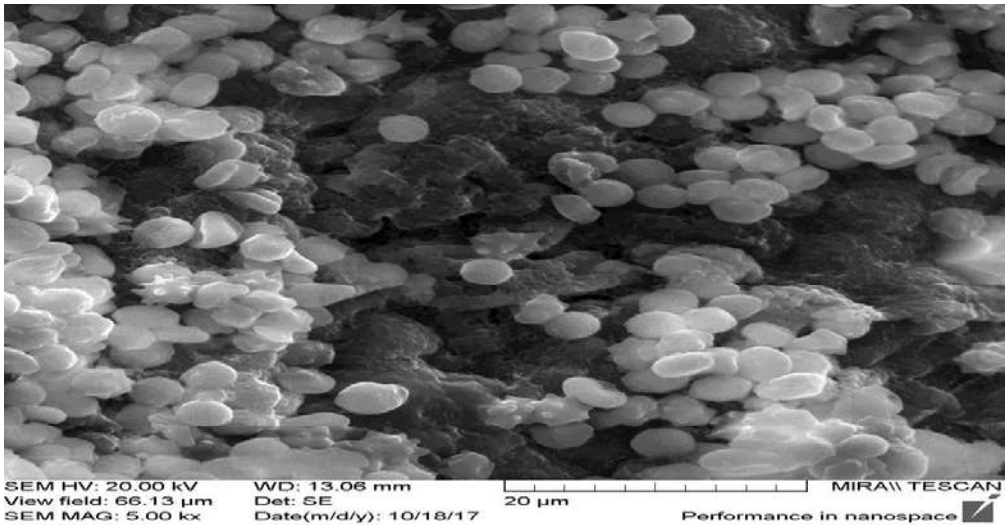


Figure 8 – Surface examination of liver tissue under a scrutiny magnifier x 20 µm

Furthermore, no alterations in cellular organelles were observed after 30 days. Nonetheless, the indications of lipid dystrophy were evident. When observed beneath a scrutiny magnifier, external entities with a gritty texture were visible on the surface of liver tissues. Isonicotinic acid hydrazide induces certain modifications within the liver. Lipid dystrophy stayed one month after isonicotinic acid hydrazide intake. Lipidoses result from the accumulation of fat, caused primarily by hypoxia.

Consequently, by using isonicotinic acid hydrazide, histopathological alterations in the liver and kidneys of young cattle were reflected in protein, lipid dystrophy and fat infiltration of hepatic cells, mitotic activity of their nuclei, ultrastructural changes with mitochondrial swelling and lipid droplets within an enlarged bulge, the lipid bar is prominent (Table 1).

Table 1 – Changes in subcellular structure of tissue cells following administration of BCG vaccine

Characteristic	T-cell	Angiotensin I / II	Organisms	Cell membrane	Foot cell	Ic
Textured Cytoplasmic Reticulum	-	-	-	-	+	+++
Silky Cytoplasmic Reticulum	-	-	-	+	+	-
Metabolic	+++	+++	+++	-	-	-
Desmosomes	-	-	-	-	-	-
Digital compact particles	+++	+++	+	+	+++	-
Glucose nodules	-	+++	+++	+++	+++	-
Lipid pigment nodules	+++	-	+++	+++	+++	-
Remaining vesicles	+++	+++	+++	+++	+/-	-
Note: *IC is an indistinguishable cell, – =not found, + / – = sometimes, +=in small quantities, ++=normal, + + + = in large quantities. (AT I/II – alveolocytes of the first and second types)						

The presence of Melanosome and starch particles within cells. was observed consistently for one, two, months after the administration of the BCG vaccine, and electron-dense granules were also found in significant amounts.

Additionally, hemodynamic changes in the cerebral cortex, liver, kidneys, lungs, heart, and gastrointestinal tract were detected as a result of isoniazid and poisoning. Furthermore, dystrophic alterations were noted in the central nervous system, hepatocytes, and other organs.

This data suggests that the accumulation of free acetylcholine and increased permeability of the cell membranes of osmoregulatory and electro genic organs are responsible for the increase in acetyl cholinesterase activity. In rabbits administered isoniazid in utero for 30 days, an increase in cholesterol in the blood was observed.

In animals exposed to isoniazid, regardless of their characteristics and dosage, signs of poisoning appear after 30-40 minutes. Isoniazid also has a negative effect on liver function. During the study, the number of lysosomes in the cell increased, and the blood vessels that supply microcirculation in the thalamus expanded slightly. The number of reticular cells and plasmablasts also increased, with the plasma cell nuclei appearing darker in color, and the number of nucleoli growing. The number of macrophages also increased.

In the kidneys, mesangial cells in the renal capillary tufts increased in size, endothelial cells lined the blood-contact area of the capillaries, and monocytes surrounded the capillary junctions. The glomerular device, formed by afferent and efferent arterioles, also increased in size. The epithelial cells of the distal segment of the nephron were thickened, and the intercellular space was extended. Juxtaglomerular granular cells were found near the wall of afferent and, in some cases, efferent arterioles.

Conclusion

Morphological changes within the body after taking Isoniazid were watched within the hepatic renal organs, entry into liver cells, nuclear division in their nuclei, cleavage of cellular components, fatty degeneration, and relationship of the degenerative prepared uncovered.

Ultra-structural structure of the calves' liver taking Isoniazid decreased hepatocyte microfibre, endoplasmic reticulum bulge, and little moulded mitochondrial cores deteriorated within the cell, and core pores were noticeable. The entrance of lipid beads in hepatocytes causes this. The pathogenic impact of the improvement of moderate touchiness can cause such a sign.

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МРНТИ 68.41.31
УДК 614:31:636.932.2
DOI: 10.52269/22266070_2023_2_16

ӨЗЕН ҚҰНДЫЗЫ СОЙЫС ӨНІМДЕРІНІҢ САПАСЫ МЕН ҚАУІПСІЗДІГІ ЖӘНЕ ВЕТЕРИНАРИЯЛЫҚ САНИТАРИЯЛЫҚ САРАПТАМАСЫ

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Мақалада саятшылар мен аңшылардың талғап жейтін асы, кәсіби ауланатын жануар болып табылатын өзен құндызы сойыс өнімдерінің қауіпсіздігі мен сапасы және ветеринарлық