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# MORPHOLOGICAL CHARACTERISTICS OF STRUCTURAL COMPONENTS OF RAT KIDNEYS UNDER THE ACTION OF FOOD SUPPLEMENTS

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The study provides a comprehensive, in-depth, and systematic analysis of the structural and functional characteristics of the macro- and microscopic organization of rat kidneys under normal conditions, and establishes in detail the pathogenetic mechanisms underlying structural remodeling of excretory system tissues under the toxic effects of the synthetic food dye Ponceau 4R. To fully achieve this aim, the study addresses a complex of interrelated tasks, beginning with a fundamental description of the histotopographic organisation of the intact kidney of the laboratory rat as a reference experimental model. This stage involves a detailed examination of the unilobar architectonics of the organ, the spatial distribution of superficial, midcortical and juxtamedullary nephrons, the relative proportions of their loops, and the microscopic organisation of the renal corpuscle and of the system of convoluted and collecting tubules. It also includes a thorough investigation of the cytotoxic and nephrotoxic effects of the food additive Ponceau 4R at the cellular and tissue levels. This encompasses the elucidation of the molecular mechanisms of damage to the components of the renal filtration barrier, the mechanisms of induction of oxidative stress in renal tissue, the initiation of apoptosis of the epithelial cells of the proximal tubules, and the aggregation of serum albumin under the action of dye metabolites. The final aspect is the formation of an integrated morphological picture of the pathological changes and haemodynamic disturbances in the kidneys, which will make it possible to provide scientific justification of the biological risks of consumption of this food additive and to create a sound fundamental theoretical basis for understanding the pathogenesis of alimentary nephropathy and for the further development of strategies for morphological correction of the disturbances detected.

**Key words:** kidneys, rats, food additives, Ponceau 4R, nephrotoxicity, excretory system organs, oxidative stress, histological analysis, renal corpuscle, tubular epithelium.

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# МОРФОЛОГІЧНА ХАРАКТЕРИСТИКА СТРУКТУРНИХ КОМПОНЕНТІВ НИРОК ЩУРА ПРИ ДІЇ ХАРЧОВИХ ДОБАВОК

Метою огляду було узагальнити сучасні наукові дані щодо макро- та мікроскопічної організації нирок щура як експериментальної моделі, а також проаналізувати відомі механізми токсичного впливу синтетичного харчового барвника Ponceau 4R на нирки. У роботі систематизовано дані про будову нефрона, ниркового фільтра, канальцевого апарату та особливості кровопостачання нирок щура. Окрему увагу приділено відомостям про цитотоксичність Ponceau 4R, індукцію оксидативного стресу, ушкодження клітин ниркового походження і потенційні ризики тривалого харчового надходження барвника. Наведені дані підтверджують доцільність подальших морфологічних і морфометричних досліджень нефротоксичності Ponceau 4R.

**Ключові слова:** нирки, щури, харчові добавки, Ponceau 4R, нефротоксичність, органи видільної системи, оксидативний стрес, гістологічний аналіз.

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The current stage of development of the food industry is characterised by the widespread use of various synthetic additives, among which dyes occupy a special place [9, 13, 26]. One of the common representatives of this group is Ponceau 4R (E124), a synthetic bright-red dye applied in beverages, confectionery, meat products and pharmaceutical preparations [7, 13]. Although this additive is officially permitted in many countries, the question of its long-term effect on the human body remains the subject of active scientific debate because recent data indicate the potential of synthetic dyes to provoke allergic, behavioural, inflammatory and organ-specific toxic effects [7, 9, 18].

The kidneys play a leading role in maintaining homeostasis by regulating electrolyte and fluid balance and by performing excretory, metabolic and endocrine functions [11, 14, 29]. Renal tissues are sensitive to xenobiotics because a substantial volume of blood passes through the kidneys, and glomerular filtration and tubular reabsorption can promote the accumulation of chemical substances and their metabolites in nephron segments [14, 22]. Therefore, investigation of renal morphological changes under conditions of exogenous exposure to food additives is an important task for morphology and pathophysiology, as it helps clarify early mechanisms of alimentary diseases of the excretory system.

The use of laboratory rats as an experimental model in biological research is a scientifically justified and widely accepted approach [11, 27]. This is due to the availability of the model, the possibility of standardised experimental conditions, and anatomical and physiological similarities with humans that allow toxicological findings to be interpreted in a biomedical context [11, 27]. A detailed analysis of the normal structural organisation of the rat kidney, including its architectonics, nephron distribution and blood supply, provides a necessary basis for the correct evaluation of pathological deviations [5, 6, 23].

Despite the substantial number of scientific studies, the specific effects of Ponceau 4R on structural components of renal tissue remain insufficiently elucidated. Available evidence includes data on oxidative stress, cytotoxicity in kidney-related cells, protein aggregation and systemic toxic effects, whereas detailed morphological and morphometric investigations of the renal corpuscle and tubular epithelium remain fragmentary [17, 32, 34]. The lack of an integrated understanding of the sequence and nature of structural remodeling in the organs of the excretory system under the influence of synthetic dyes underlies the relevance of this review.

**The purpose** of the study was to summarise current scientific concepts regarding the macro- and microscopic structural features of rat kidneys and to analyse the pathogenetic mechanisms underlying the effects of the synthetic food additive Ponceau 4R on renal tissue and other organs of the excretory system.

**Materials and methods.** The systematic review of the scientific literature was conducted to achieve the study aim, which involved a comprehensive evaluation of rat kidney structure and the impact of the food additive Ponceau 4R on the excretory system. Information retrieval was performed in PubMed, Web of Science, Scopus, and Google Scholar. The last search was performed on 7 June 2026. Publications from 2021 to 2026 were included in the reference list; sources published before 2021 were excluded, except for historically important data mentioned only in the text when necessary. The analyzed sources comprised English- and Ukrainian-language full-text original experimental studies and review articles published in peer-reviewed journals. The search strategy used the following terms and combinations: morphology of rat kidneys, nephron histology, macro- and microscopic anatomy of the excretory system, renal corpuscle, tubular system, renal barrier, experimental rat models, food additives, synthetic dyes, Ponceau 4R, E124, nephrotoxicity, in vitro cytotoxicity, oxidative stress in kidneys, serum albumin aggregation, and dye elimination mechanisms. Inclusion criteria were full-text peer-reviewed publications with morphometric data on intact rat kidneys or reliable results on pathogenetic mechanisms of renal tissue damage associated with Ponceau 4R. Conference abstracts, non-peer-reviewed preprints, duplicate publications, papers without DOI, and works not directly related to structural remodeling or nephrotoxicity were excluded. Since the present study is a theoretical review based on publicly available scientific information, it did not require approval from a bioethics committee. Source selection was performed according to the PRISMA approach. At the initial stage, 191 publications were identified; after removal of 35 duplicates, 156 records were screened by titles and abstracts. Then 74 full-text articles were assessed for eligibility, and 37 publications were included in the final review (Table 1).

Table 1

**Simplified PRISMA Flow**

| Stage | Description | Number of Records / Studies |
|---|---|---|
| 1. Identified | Total number of records found in scientometric databases using keywords related to rat kidney structure and Ponceau 4R nephrotoxicity | 191 |
| 2. Duplicates Removed | Number of identical publications removed before screening began | 35 |
| 3. Screened (Title/Abstract) | Number of records screened by title and abstract after removal of duplicates | 156 |
| 4. Assessed for Eligibility (Full-text) | Number of full-text articles analysed for compliance with methodological criteria and the presence of the necessary morphological data | 74 |
| 5. Included in Review | Total number of primary scientific studies finally included in the systematic review and used in the text of the article | 37 |

**Results of the study and their discussion.** Animal studies represent an indispensable stage in biomedical sciences, since they make it possible to investigate the development, diagnosis and treatment of diseases by simulating pathological conditions similar to those of humans. This makes it possible to study the toxicological properties and side effects of new medicinal products and medical equipment before their use in humans, which is of great importance from the ethical and safety points of view [27].

At present, the laboratory rat model has gained wide application in biomedical research. This is due not only to its accessibility, undemanding maintenance and rapid reproductive cycle, but also to the considerable physiological and anatomical similarity of its organism to that of humans [11].

Information on the structural features of the anatomical organisation of the rat kidney can be drawn from the studies of researchers engaged in examining and comparing the structure of the organs of various laboratory animals and/or in the experimental modelling of various pathological conditions of the excretory system.

The kidneys are critically important organs maintaining the chemical and fluid homeostasis of the organism by eliminating waste products and controlling excess of dissolved substances and fluids [14]. To ensure continuous filtration and reabsorption, the kidneys receive an exceptionally high blood flow, which constitutes approximately 25 % of the cardiac output [15].

The kidneys also play an active role in regulating metabolic processes through the synthesis of erythropoietin, renin, and calcitriol (the active form of vitamin D) [11].

Rat kidneys are paired, bean-shaped organs of dark reddish-brown color, located retroperitoneally in the sublumbar region [5]. Their position is characteristically asymmetric: the right kidney lies more cranially (at the level of the 2nd-4th lumbar vertebrae) and is adjacent to the liver and duodenum, whereas the left kidney is positioned more caudally (at the level of the 3rd-5th lumbar vertebrae) and contacts the spleen, stomach, and intestines. Unlike in mice, the right kidney in rats exhibits a distinctive visceral attachment to the right lateral lobe of the liver, known as the hepato-renal ligament [5].

The rat kidney consists of an outer cortical layer (Cortex) and an inner medullary layer (Medulla), separated by the corticomedullary junction [23]. A characteristic feature in rats is the marked predominance of the medulla: the average thickness of the cortex is approximately 2.8 mm, whereas the medulla reaches about 7.2 mm. The medulla, represented by a single pyramid, has a complex structure and terminates in the renal papilla (Papilla renalis). At the apex of the papilla, forming an oval region known as the (area cribrosa), approximately 20 circular openings (foramina papillaria) with diameters ranging from 70 to 140 μm are present [23].

The nephron constitutes the principal structural and functional unit of the kidney and consists of the renal corpuscle and the tubular system [19, 31].

The renal corpuscle, located in the cortex, is spherical and comprises a glomerular capillary tuft enclosed by the bilayered Shumlyansky–Bowman capsule [31]. The outer parietal layer of the capsule consists of simple squamous epithelium, whereas the inner visceral layer is formed by podocytes [30].

The nephron tubular system exhibits distinct histological features that correspond to its functional roles. Proximal convoluted tubules are lined by simple columnar or cuboidal epithelium with a well-developed apical brush border, which markedly increases the surface area for reabsorption [31]. Distal convoluted tubules are lined by simple cuboidal epithelium lacking a brush border [30, 31].

They stain more lightly than proximal tubules and are less numerous in the cortical region [23, 31].

The loops of Henle, which include thin descending and ascending limbs extending into the medulla, as well as the collecting ducts, also lack a brush border [23]. The cells of the collecting ducts are lined by cuboidal epithelium that becomes columnar toward the papilla. The boundaries between these cells are typically well defined [31].

The renal cortex contains renal corpuscles and proximal convoluted tubules. The medulla of the rat kidney is divided into two layers — outer and inner — the latter terminating at the papilla of the pyramid. The outer medulla is further subdivided into outer and inner stripes. The outer stripe of the outer medulla contains distal segments of proximal tubules, thick ascending limbs, distal tubules, and collecting ducts. The inner stripe of the outer medulla, as well as the inner medulla, contains collecting ducts and segments of nephron loops with distal tubules, interspersed with vasa recta (straight vessels) and stromal cells [22].

The anatomical structure of the rat kidney is unilobar and unipapillary, as it contains a single large renal papilla that extends deeply into the renal pelvis. This structure differs markedly from the multipapillary kidney of humans. Despite this, the zonal architecture of the rat kidney resembles that of the human kidney. In both rats and humans, superficial and midcortical nephrons (with short loops of Henle) and juxtamedullary nephrons (with long loops of Henle) are present; however, in rats, long loops predominate over short ones at a ratio of 3:1, whereas in humans the ratio is approximately 7:1 [6].

At the electron-microscopic level, the renal filter, which ensures the formation of the primary urine, is a complex multilayered structure [30]. It is located between the blood in the capillaries of the glomerulus and the urinary space of the Shumlyansky–Bowman capsule and consists of three principal components:

1. Fenestrated capillary endothelium. Endothelial cells possess thin peripheral regions with fenestrations that ensure high permeability to blood plasma while preventing the passage of blood cells [30].

2. Trilaminar basement membrane. Situated between the endothelium and podocytes, it comprises an electron-dense central layer and two lighter peripheral laminae. The basement membrane serves as the principal barrier preventing filtration of large proteins [30].

3. Podocytes of the visceral leaflet of the Shumlyansky–Bowman capsule. These specialised cells have primary processes (cytotrabeculae), from which numerous small secondary processes (cytopodia) extend [23, 30].

Narrow filtration slits formed between the cytopodia constitute the final barrier to the passage of macromolecules [30].

Nephron structure mediates the response to acute hyperkalemia. Increased potassium ($K^+$) secretion occurs in the connecting tubules (CNT). Peritubular $K^+$ attenuates sodium ($Na^+$) reabsorption in the proximal convoluted tubules (PCT), the thick ascending limb of the loop of Henle, and the distal convoluted tubules (DCT). However, tubuloglomerular feedback (TGF), mediated by the macula densa, limits transmission of proximal effects. Consequently, the effect occurring in the DCT is critical for increasing $Na^+$ delivery to the CNT. Hyperkalemia also reduces ammoniagenesis, which, as proposed by current models, increases the pH of principal cells in the CNT, thereby enhancing the conductance of the epithelial $Na^+$ channel (ENaC) and the renal outer medullary $K^+$ channel (ROMK), ultimately promoting $K^+$ excretion [35].

The kidneys serve as a major source of ammonia ($NH_3$), which acts as a principal buffer for acid excretion. Modeling of ammonia transport in the rat kidney has shown that ammonia concentration in the interstitial space of the cortical labyrinth (the region containing glomeruli and convoluted tubules) is likely several times higher than systemic arterial ammonia levels. This elevated local concentration enhances ammonia secretion in both proximal and distal convoluted tubules, while cellular uptake occurs via $Na^+/K^+$-ATPase activity. Trapping of ammonia within the medulla represents a key structural and functional mechanism that redirects ammonia from the renal vein into the urine, thereby ensuring effective buffering capacity [35].

Postnatal maturation of renal structures is heterochronic. New nephron primordia develop in the cortex until approximately the fifth postnatal day, and the cortex reaches maturity by day 15. In contrast, the medulla matures considerably later, around day 36 after birth. During this process, tubular diameter increases, and loops of Henle, which are relatively longer at certain immature stages, become proportionally shorter in adulthood. In adult kidneys, Bowman's capsule contains a greater amount of collagen fibers and exhibits a distinct narrow urinary (capsular) space surrounding the glomeruli [33].

The kidneys possess a complex innervation system that includes both sympathetic (efferent) and sensory (afferent) nerve fibers [29].

Sympathetic innervation is most densely distributed in the afferent arterioles and is also present in the proximal and distal tubules [29].

The activity of sympathetic nerves leads to a decrease in the glomerular filtration rate, an increase in sodium reabsorption and stimulation of renin release [29].

Afferent sensory nerves transmitting information from the kidneys to the brain are most abundant in the renal pelvis and play an important role in reflex regulation. For example, they contribute to the inhibition of sympathetic outflow, thereby promoting natriuresis and diuresis [29]. This complex neural network highlights that renal function is not autonomous but is tightly integrated with the central nervous system, enabling the organ to adapt to changes in overall homeostasis.

In addition to epithelial cells, the renal structure of rats includes a stable population of immune cells. In particular, resident renal macrophages, identified by CD81 and C1q markers, contribute to the maintenance of tissue homeostasis. A key structural and biological feature is that these resident macrophages sustain their population through self-renewal and demonstrate minimal turnover or recruitment from peripheral blood. This property, previously confirmed in mice, is conserved in at least two species, emphasizing the autonomous nature of this cellular population within the renal parenchyma [37].

Renal structure is not static and undergoes significant age-related changes. Kidney aging in rats is associated with progressive sclerosis, fibrosis, and degeneration. In aged animals, glomerular asymmetry and hypertrophy are observed, along with tubular atrophy, leading to an overall decline in renal function. These changes are an important consideration in experimental interpretation, as age may influence susceptibility to toxic agents [24].

Exposure to various experimental factors can induce significant structural and functional alterations in rat kidneys. For example, in offspring of rats exposed to passive tobacco smoke during pregnancy, a marked reduction in the number and size of renal corpuscles was observed, indicating impaired nephrogenesis [1]. Moreover, thickening of Shumlyansky–Bowman capsule, pronounced glomerulosclerosis, and arteriolosclerosis indicating vascular sclerosis were reported [1].

Tubular analysis revealed protein degeneration, nephrocyte atrophy, and the presence of protein casts within the tubular lumen, all of which serve as markers of epithelial injury. These changes may result from hyperfiltration and fibrosis and may ultimately contribute to the development of renal failure [19].

The literature review demonstrated that the anatomical and histological structure of rat kidneys shows a high degree of similarity to that of humans, making rats a reliable and widely used experimental model. Rat kidneys are unipapillary, exhibit asymmetrical positioning, and possess a distinctive hepatorenal ligament. Their functional unit — the nephron — consists of the renal corpuscle and a tubular system, whose histological characteristics directly determine their roles in filtration, reabsorption, and secretion. At the ultrastructural level, the renal filtration barrier represents a complex trilaminar system, and its efficiency is maintained by the diameter difference between the afferent and efferent arterioles.

However, the structure of rat kidneys is not static. It undergoes dynamic changes throughout life, ranging from postnatal maturation to progressive degeneration and fibrosis in aging. In addition, external pathogenic factors may accelerate these processes, inducing structural alterations that lead to organ dysfunction.

Profound understanding of these structural features and their changes is critically important for the correct planning and interpretation of the results of biomedical studies that use rats as an experimental model.

Food colorants, which enhance the visual appeal of products, are an integral component of the modern food industry. Among them, synthetic dyes such as Ponceau 4R (E124) occupy a special place due to their chemical stability, bright coloration, low production cost, and high stability [26].

Ponceau 4R is a synthetic red food dye, also known as Cochineal Red A. It is the trisodium salt of 1-(4-sulfonatonaphthylazo)-2-naphthol-6,8-disulfonic acid (chemical formula $C_{20}H_{11}N_2O_{10}S_3Na_3$; CAS number 2611-82-7; molecular weight 604.48) (FAO/WHO Codex Alimentarius, 2024), containing auxiliary components such as sodium chloride and/or sodium sulfate as major non-coloring constituents. Ponceau 4R is described as a sodium salt [16].

This dye is added to a wide range of products, including flavored beverages and fermented dairy products, jams, jellies, confectionery, soups, condiments, sauces, and meat products, particularly sausages [13, 32].

Since the chemical structure of Ponceau 4R includes toxic and potentially carcinogenic aromatic ring structures and azo functional groups [26], the scientific literature contains numerous works investigating various methods for its detection in foodstuffs and medicinal products [10, 20, 25, 36].

The legal status of Ponceau 4R varies significantly across countries. In the United States and Canada, the use of this dye is prohibited, whereas in the European Union it is permitted within restricted concentration limits [4]. Regulatory authorities such as the U.S. Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) are responsible for assessing the safety of food additives [9]. The acceptable daily intake (ADI) for Ponceau 4R established by EFSA is 0.7 mg/kg body weight, whereas FAO/WHO assessments set the ADI at 4 mg/kg [7].

This discrepancy in evaluations underlines the need for additional studies and revision of the existing standards. Despite the established limits, safety concerns remain, since, as researchers note, toxicity is dose-dependent, and the monitoring of compliance with the standards is complicated, especially for imported products [9].

Experimental studies indicate that excessive consumption of Ponceau 4R poses a significant risk to human health, inducing a wide range of adverse effects that extend beyond the excretory system [12].

Ponceau 4R has been associated with hyperactivity and attention disorders in children [3, 18].

Recent animal evidence summarised in the review by Amchova et al. showed that rats receiving a mixture of sodium nitrite, monosodium glutamate and Ponceau 4R for 16 weeks developed alterations in the structure and thickness of the duodenal wall [7]. Although the dose of Ponceau 4R was high (5 mg/kg), these findings may indicate a synergistic toxic effect of food additives commonly used in meat products [7].

Consumption of Ponceau 4R may trigger allergic reactions, asthma, urticaria, migraines, and anxiety. The dye is considered potentially carcinogenic due to its chemical structure [12, 26]. Genotoxic effects of Ponceau 4R on human peripheral lymphocytes have been confirmed in *in vitro* studies, particularly at high concentrations [21].

Experimental data obtained in rats after prolonged administration of Ponceau 4R in combination with other food additives also indicate systemic endocrine and morphological responses, including changes in the adrenal cortex [2].

Although most azo dyes are eliminated via the kidneys, *in vivo* studies specifically addressing the direct effects of Ponceau 4R on renal tissue remain limited in the literature. Nevertheless, available data clearly indicate the high cytotoxicity of this dye toward renal cells and its ability to induce both structural and physiological disturbances.

In the studies by Taheri et al., particular attention was given to the effects of Ponceau 4R on the excretory system. This is explained by the fact that the kidneys represent the primary organ responsible for the elimination of such dyes from the body. Due to its low molecular weight and high hydrophilic nature, Ponceau 4R and its metabolites efficiently undergo glomerular filtration and are rapidly excreted in urine. While this process facilitates detoxification of the organism, it simultaneously renders renal tissue particularly vulnerable to the toxic effects of the dye.

Cytotoxicity studies on the human embryonic kidney cell line (HEK293), selected due to its relevance to dye excretion, demonstrated that Ponceau 4R is highly toxic to nephron-related cells. At a concentration as low as 5 ng/mL, it induced the death of up to 80% of cells. This level of toxicity was significantly higher compared with other dyes tested in the same experiment, including Sunset Yellow and Tartrazine [34].

The mechanism of Ponceau 4R toxicity in renal cells is associated with its chemical properties. Researchers suggest that the toxic effect is linked to incomplete tautomeric conversion of the dye in the cellular environment. Ponceau 4R can exist in two forms — azo and hydrazo — and its dynamic equilibrium depends on environmental polarity. Under conditions simulating the cellular

environment, accumulation of the hydrazo form occurs, which is considered to be the principal cause of cytotoxicity [34]. This accumulation induces oxidative stress, which is manifested by an increase in reactive oxygen species (ROS).

Oxidative stress, in turn, leads to mitochondrial dysfunction, damage to cellular membranes and DNA, and ultimately triggers apoptosis (programmed cell death) [34].

The study by Silva et al. in rats administered Ponceau 4R at a dose of 7.5 mg/kg body weight for 28 days documented systemic pathological changes affecting the excretory system. Significant increases in nitric oxide (NO) and malondialdehyde (MDA) levels were observed, both of which are key biomarkers of oxidative stress and inflammation that can contribute to renal tissue damage. Histopathological and physiological abnormalities were identified in both the kidneys and liver of treated animals, indicating a direct nephrotoxic and hepatotoxic effect [32].

Ponceau 4R has also been shown to stimulate the production of reactive oxygen species (ROS) and alter the redox balance of organs, representing an early event preceding functional impairment of the excretory system [28].

Studies on various model organisms, including cucumber seeds (*Cucumis sativus*), *Artemia salina* cysts, and *Danio rerio* embryos, demonstrated that Ponceau 4R (E124) induces both an increase in reactive oxygen species and modulation of antioxidant capacity, indicating a high risk of oxidative stress [28].

Ponceau 4R reduced cell viability *in vivo*, confirming cytotoxic effects previously observed in rapidly proliferating cancer cell lines. Metabolic and physiological alterations are also supported by indirect effects such as reduced root length in *Cucumis sativus* and changes in shoot-to-root ratio, which may impair water and nutrient uptake capacity [8].

Another mechanism of toxicity relevant to the renal filtration apparatus (which includes protein components) involves interactions with proteins. Ponceau 4R has been shown to induce aggregation of human serum albumin (HSA) *in vitro*. The dye causes modification of the protein's secondary structure, converting α-helical conformations into β-structures, leading to the formation of amorphous aggregates [17].

Protein aggregation is responsible for the development of many severe diseases [17]. Although the study was conducted *in vitro* with serum albumin, disruption of protein structure and its aggregation may be relevant in the context of glomerular diseases, where the functional integrity of the filtration barrier depends on the stability of protein components.

Analysis of available literature indicates the harmful effects of Ponceau 4R on the human body. Numerous studies confirm its adverse impact on various organs and systems, including the lungs, gastrointestinal tract, and nervous system. At the same time, the number of studies addressing the nephrotoxicity of this compound remains extremely limited. Considering the potential toxicity of Ponceau 4R and its widespread use in the food industry, further investigation of its effects on the structure and function of renal tissues is of particular scientific and practical importance. Thus, the present study is relevant and addresses an existing gap in knowledge regarding the long-term effects of Ponceau 4R on the excretory system.

## Conclusion

The literature review confirms that the rat kidney is a valuable experimental model for studying excretory-system pathology because its nephron organisation, filtration barrier and tubular apparatus allow assessment of structural responses to xenobiotics. Ponceau 4R is a widely used azo dye whose potential toxicity is associated with oxidative stress, inflammatory reactions, cytotoxicity toward kidney-related cells and interactions with protein structures. However, direct in vivo evidence on Ponceau 4R-induced renal remodeling remains limited, and available data are often obtained at high doses or in combined-additive models.

*Prospects for further research. Further studies should focus on dose-dependent morphological and morphometric changes in the renal corpuscle and tubular epithelium, comparison of short- and long-term exposure, and evaluation of protective agents capable of reducing oxidative damage and stabilising renal histoarchitecture.*

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