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POISONOUS PLANTS AND PHYTOTOXICOSES IN HORSES
(review)

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Abstract

A large number of plants contain chemical compounds that have a toxic effect on animals (E.M. Kurenkova et al., 2018). Feed-born phytotoxins cause severe pathology in horses. Phytotoxins are diverse in species composition, distribution, mode of action and lethal effect. Poisoning of horses by poisonous plants is a relatively common veterinary problem that can occur when a fresh plant is ingested by an animal on pasture or when the plant contaminates hay, silage and other feed (F. Caloni et al., 2015). Plant toxicity is also a serious problem, as animal poisoning results in significant economic losses (L. Curtis et al., 2019). Depending on the degree of toxicity and the amount of plant eaten, the effect varies from mild illness to disruption of the activity of organs and body systems, which can lead to animal death (M. Wickstrom, 2002). Poisoning caused by poisonous plants is difficult to diagnose and differentiate from other pathologies, since clinical signs are usually not specific and can be observed in other diseases (K.E. Panter et al., 2012). Data on the true incidence of equine poisoning by plant toxins are sparse or absent due to lack of centralized poisoning reporting and monitoring system in place (K. Welch, 2019). Despite the fact that most toxic plants have an unpleasant taste for horses, there are many factors that increase the risk of poisoning, e.g., the influence of the growing season on the taste of some poisonous plants, lack of feed on pasture, toxic plants getting into the hay, monotonous habitat, curiosity, etc. (F. Caloni et al., 2015). It is important to constantly update the knowledge of veterinarians and animal owners about the poisonous plant diversity, phytotoxins, and phytotoxicoses. The review summarizes the most common plant species in Russia which causes poisoning in horses. The places are indicated where plants that are poisonous to horses grow, the mechanisms of action of the toxic substances they contain and their clinical effects in animals are described in detail, including disturbances in the digestive, cardiovascular, excretory, respiratory and nervous systems and many other sings. Poisonous plants are classified according to the mechanism of action of toxic substances into groups containing alkaloids, neurotoxins, photosensitizing substances, cyanogenic glycosides, and cardiac glycosides (M.I. San Andrés Larrea et al., 2024). The need for careful monitoring of the botanical composition of pastures and hay, and avoiding accidental consumption of poisonous plants by horses, is emphasized.

Keywords: poisonous plants, horses, phytotoxins, mechanism of toxicity, clinical signs, habitat

A potential threat to the health of horses arises from toxic compounds in plants eaten by animals due to violations in the management of stables and pastures [1], which can lead to decreased productivity, exhaustion, chronic intoxication and even death of the animal [2]. The increasing rate of weed spread in hayfields and pastures around the world is leading to the colonization of new regions by these species, posing additional threats to animals [3, 4]. There are hundreds of plant species that can be toxic to horses, with some only growing in

certain areas. To prevent poisoning, horse owners and managers of horse breeding enterprises need to be informed about species that have a toxic effect on animals, so that when studying the botanical composition of pasture grass, hayfields and areas adjacent to the stable, they can identify potentially dangerous plants [5].

In Russia, according to 2010 data, 4,730 species of meadow and pasture plants have been studied, more than 750 are classified as poisonous and harmful [6], and the phytotoxins contained in many of them cause poisoning of horses [7]. Poisonous plants are classified according to the target organ and the corresponding effect caused by the toxins they contain (cardiotoxic, hepatotoxic, neurotoxic, teratogenic and other effects), according to the active substances (containing cyanides, nitrates, oxalates, alkaloids, glycosides, etc.), by family and genus [8]. The formation and accumulation of toxic substances in plants is influenced by a number of factors, such as the growing area, soil, climatic and weather conditions, and phases of the growing season [9].

When horses are exposed to phytotoxins, pathological processes develop, characterized by varying severity and a variety of clinical signs. Providing information to horse owners and veterinarians about the potential hazards of feed contamination from poisonous plants can be a measure that will prevent animal poisonings and assist to performe anamnezing and diagnosis. Poisoning by poisonous plants, as a rule, does not have a specific treatment, and therefore the survival of the animal largely depends on supportive and symptomatic care. In some cases, the causes of death of the animal are not diagnosed until autopsy and identification of plant fragments in the stomach [10, 11]. Educating equine professionals about toxic plants and understanding the factors that influence the risk of poisoning will help ensure animal safety [12].

This review provides information on phytotoxins in plants that are poisonous to horses and various ways of poisoning. Here, we also summarize data on the nature of the effects of different classes of phytotoxins and describe the clinical signs and physiological and biochemical changes in acute and chronic toxicosis.

In most cases, horses avoid eating poisonous plants in toxic quantities. However, some plants are readily eaten by horses, and some species can cause poisoning if accidentally consumed in small amounts. The toxicity of some species is influenced by seasonal conditions, and therefore their negative effects on animals vary depending on the time of year. Since most poisonous plants have an unpleasant taste, horses try not to eat them, but with a lack of alternative feed, animal's feed selectivity decreases. Keeping horses in a monotonous environment that does not provide sufficient physical activity and/or sensory stimulation and the lack of satisfied zoosocial needs increase the likelihood of consuming poisonous plants out of boredom. Moving horses to a new location where the botanical composition of the pasture is unfamiliar to the animal may be another reason for eating plants that contain toxic substances or their precursors [13].

Poisonous plants should be considered a potential cause of disease if pasture feed supplies are poor due to overgrazing, drought, or poor early-season growth, if the animals have recently been moved to a new pasture, when hungry animals were released to new pasture, if a new feed or batch of feed (e.g., hay) are used [14]. The presence of such plants in hay can pose a serious threat to most stabled horses, as they generally do not have the choice unlike the animals that have access to pasture. Some horses will separate hay, refusing to consume suspicious plants, but most animals tend to eat them, despite the specific taste or smell, because due to the lack of constant access to hay they demonstrate a high rate of eating. A horse that is not very hungry can also eat hay contaminated with poisonous plants, since the intensity of the offending taste or smell can be reduced during drying without reducing toxicity [15].

Plant poisons, or phytotoxins, are products of plant metabolism and most often perform protective functions, scaring away possible consumers, since they have the properties of biological contaminants, the compounds that have high biological activity with a negative effect on animals [16]. Phytotoxins include a group of diverse low- and high-molecular bioactive compounds which include non-proteinogenic amino acids, isoprenoids, glycosides, alkaloids, phenolic compounds, steroids, lectins and other substances [17].

Plants containing alkaloids. Alkaloids are secondary metabolites found in approximately 20% of plant species. Alkaloids represent a diverse group of compounds linked by the presence of a nitrogen atom in a heterocyclic ring, including pyrrolidine, pyrrolisidine [18], tropane [19], pipyridine [20, 21], quinolizidine [22], indolizidine, quinoline [23] and other groups [24].

Pyrrolizidine alkaloids are one of the most important classes of naturally occurring toxins due to their widespread occurrence and high risk of accidental animal consumption of contaminated feed [25]. More than 350 pyrrolizidine-based alkaloids have been found in plants, with some plants containing multiple types of toxins. Pyrrolizidine alkaloids are a large group of cytotoxic [26], neurotoxic [27], tumorigenic [28], hepatotoxic, pneumotoxic and genotoxic compounds [29-31].

Pyrrolizidine alkaloids themselves are not toxic, but when absorbed from the gastrointestinal tract (GIT), they reachthe liver, their first target organ. The of hepatotoxicity caused by pyrrolizidine alkaloids is due to several mechanisms, such as activation of pyrrole ester, formation of reactive oxygen species, and activation of glutathione-degrading enzymes. The latter are found in most tissues, especially in high concentrations in the liver, and play an extremely important role in protecting hepatocytes, red blood cells, and other cells from toxic damage [32-35]. Pyrrolizidine alkaloids are also metabolized by liver microsomal enzymes to pyrrole derivatives which inhibit replication and protein synthesis. As a result, the cells are unable to divide and instead continue to grow, forming megalocytes which are eventually replaced by fibrous tissue [36].

The extent of damage to the liver or other organs depends on the specific type of pyrrolizidine alkaloid and its amount. Pyrrolizidine alkaloid poisoning can be acute or chronic, with the acute form being extremely rare because it occurs when large amounts of toxic plants are accidentally ingested with contaminated hay or when toxic plants become the dominant species in the pasture [37]. Chronic poisoning occurs when a horse consumes small amounts of the plant over a long period. The onset of clinical signs of chronic pyrrolizidine alkaloid poisoning is delayed and does not appear until several weeks or months after initial exposure. Thus, there may be cumulative and progressive effects of repeated administration of the toxin in small doses. This makes it difficult to determine when and under what conditions a horse was exposed to toxins [38].

Liver diseases with accompanying clinical signs in the form of progressive liver failure are becoming the most common signs of pyrrolizidine alkaloidosis. Acute intoxication leads to sudden death from hemorrhagic liver necrosis and visceral hemorrhages [39]. The animal may die within a few days or weeks. Horses with significant signs of acute pyrrolizidine alkaloid poisoning rarely recover. Clinical signs of chronic intoxication in horses include deterioration of condition, anorexia, lethargy, constipation or diarrhea, hepatic encephalopathy, jaundice (yellow discoloration of the mucous membranes), bloating (colic), and behavioral changes, e.g., head shaking, yawning, aimless wandering, head resting into the wall, hyperexcitability and aggressiveness [40].

Secondary, or hepatogenic, photosensitization may occur, caused particularly by disruption of detoxification in the live of phylloerythrin, the product of

chlorophyll metabolism. Phylloerythrin is produced by intestinal microflora and, during intoxication, accumulates in the skin where due to UV activation free radicals are formed that damage cell membranes. At the initial stage, erythema of non-pigmented hairless areas (nasal tract, eyelids and visible mucous membranes) appears, and later swelling develops, turning into dermatotonecrosis [41]. As the liver gradually loses function, the symptoms intensify, and when the liver is critically damaged, liver failure progresses rapidly. As a result death can occur suddenly or after the animal remains in a prone position for a long time, which is accompanied by hepatic coma and a high blood concentration of ammonia. Less common clinical signs described in pyrrolizidine toxicoses are inspiratory dyspnea in ponies due to laryngeal and pharynx paralysis, and dyspnea due to interstitial pneumonia in horses [42, 43].

Tropane alkaloids are a class of bicyclic alkaloids and secondary metabolites that occur naturally in many plants of the *Solanaceae* family and have anticholinergic effects. They reduce the metabolic effects of acetylcholine, a key neurotransmitter, by acting in mammals as antagonists of central and peripheral muscarinic acetylcholine receptors and, therefore, can cause a distinct toxic syndrome [44]. More than 200 tropane alkaloids are known, but the most studied are atropine and scopolamine [41]. Symptoms associated with tropane alkaloids are dryness of the upper gastrointestinal tract and respiratory tract, constipation and colic, dilated pupils (mydriasis), changes in heart rate, and central nervous system effects such as restlessness, irritability, ataxia, seizures and respiratory depression. In severe cases, death may occur from respiratory paralysis, heart failure, or gastric rupture within minutes, hours, or days after the animal consumes the toxic plant [45].

Piperidine alkaloids are extremely toxic to adult animals and also have a teratogenic effect. The mechanism of the teratogenic potential of these compounds is the stimulation of muscle-type acetylcholine receptors with subsequent desensitization and inhibition of fetal movements, which leads to the development of musculoskeletal pathologies [46, 47]. Acute toxicoses caused by plant piperidine alkaloids are due to their ability to reduce the sensitivity of acetylcholine receptors. As a consequence, paralysis of the endings of sensory and motor neurons occurs, as well as damage to the central nervous system (first its excitation occurs, and then paralysis) [48].

In Russia, horses are especially at risk of poisoning by such species of alkaloid-containing plants as *Convolvulus arvensis* L., plants of the genus *Aconitum* L., *Colchicum autumnale* L., *Hyoscyamus niger* L., *Datura stramonium* L., *Conium maculatum* L., *Senecio jacobaea* L., *Jacobaea vulgaris* L. [24, 49].

Field bindweed is a perennial herbaceous weed in cultivated areas. Tropane and pyrrolidine alkaloids were found in its shoots and roots [50]. Horses are very sensitive to toxic substances of field bindweed that cause impaired intestinal motor function, leading to colic [51], barycardia (slow heart rate) and dilated pupils [52].

Aconites are a genus of perennial poisonous herbaceous plants of the *Ranunculaceae* family, numbering over 50 species. The plants are distributed throughout Russia, growing in damp places along river banks and along roadsides, in humus-rich soils and mountain meadows [53]. Animals generally do not eat these plants, so poisoning in the field is rare, but they may contaminate the hay. All vegetative organs of plants contain alkaloids, primarily the highly toxic aconitine, which has cardio- and neurotoxic effects due to short-term stimulation of the central nervous system (especially the respiratory center) and peripheral nerves (the endings of the motor, sensory, secretory and recurrent nerves), followed by

their oppression. The mechanism for the development of pathophysiological reactions is due to the effect of the toxin on voltage-gated sodium channels in neurons, the conduction system of the heart and muscles, which causes a constant influx of sodium (that is, persistent depolarization) and prevents adequate repolarization, leading to seizures and arrhythmias. In the heart, excess sodium influx activates calcium metabolism, and intracellular hypercalcemia increases both the inotropic effect (changes in the force of cardiac contraction) and the likelihood of arrhythmias [54]. All parts of the plants are extremely poisonous to horses. If even small amounts are ingested, severe symptoms appear within minutes, and if lethal doses are ingested, death usually occurs within 6 h. Signs of intoxication in horses include gastrointestinal symptoms, including diarrhea and colic, as well as cardiac manifestations, e.g., slow heart rate, hypotension, and arrhythmias leading to suffocation which often causes death in animals [55]. Although there is not enough information about the toxic dose of aconite, a fatal case of poisoning of horses has been reported after eating 0.075% green plants by weight, that is, only 10-12 g. The most poisonous part of aconite is the rhizome, but cases of poisoning of horses with it have not been recorded. Poisoning by abovegraound parts of the plant is possible on mountain pastures and when grazing in gardens where aconites are grown as ornamental plants. There are known cases of poisoning with silage containing aconite plants [56].

H. niger and *D. stramonium* are poisonous plants of the *Solanaceae* family and growing mainly in the European Russia. Both species are classified as weeds; they can be found near roads, near housing, in fallow lands and fields. *H. niger* grows scatteredly or in small groups, and since the plant does not form thickets, it is difficult to detect at the early stage of the growing season. Datura is rarely found as a single plant; it often forms small groups (curtains) [57]. All parts of these plants contain the tropane alkaloids hyoscyamine and scopolamine the toxicity of which persists during drying [58], ensiling and haylage [59]. Animal consumption of henbane and datura may be accompanied by bloating, difficulty breathing, convulsions, cyanosis, tachycardia, incoordination, dilated pupils, and restlessness [60].

Poisoning of horses by *D. stramonium* has been widely studied. An outbreak of intractable, long-lasting, recurrent colic due to colonic and/or cecal obstruction without any other antimuscarinic signs occcur in horses consuming hay contaminated with this plant [61]. Toxic effects of this plant have also been documented in horses fed a sunflower-based supplement heavily contaminated with Datura seeds, one horse suddenly died from acute dilatation and rupture of the stomach, and in other horse an intestinal obstruction occurred which resulted in the animal being euthanized [62]. Spontaneous intoxication was described in 34 horses after eating freshly cut corn intended for silage and heavily contaminated with young Datura plants. Intoxication was accompanied by erythrocytosis, leukocytosis, regenerative neutrophilia with a shift to the left, lymphopenia, eosinopenia, increased hematocrit, low erythrocyte sedimentation rate, hyperglycemia, bilirubinemia, hypoproteinemia and increased activity of the enzymes alanine aminotransferase and aspartate aminotransferase. Autopsies and pathological studies of two dead horses revealed toxic liver degeneration, heart damage and significant degenerative and necrotic processes in the kidneys [63].

C. maculatum contains 8 alkaloids of which the most toxic are coniine and γ-coniceine, which have nerve paralytic and teratogenic effects. This is a widespread plant growing in the temperate climate zone; its natural range in Russia covers almost the entire European part, the Caucasus and Western Siberia. The plant is found everywhere, i.e., on forest edges, water meadows, limestone slopes,

as a weed in crops and vegetable gardens, in fallow lands and wastelands, near housing, along roads and fences, in landfills [64]. All parts of the plant are poisonous, and their consumption causes respiratory failure in less than 3 h. Horses can eat young plants when other feed is not available. The toxicity of spotted hemlock persists in hay, but gradually decreases during storage. Horses can be poisoned by eating this plant in amounts as low as 0.25% of their body weight. The alkaloids contained in the plant initially have a stimulating effect, followed by long-term depression of the function of the central nervous system. Common clinical signs of poisoning in horses include nervousness, frequent urination and defecation, trembling, staggering, ataxia, hyperpnea (disturbed respiratory rhythm) and tachycardia, followed by depression and inability to rise from a prone position. Coma also develops, and the animal may collapse due to respiratory failure [65, 66]. Teratogenic effects are possible when the plant is consumed by pregnant mares [67].

J. vulgaris is found in all regions of central Russia in meadows and clearings, along forest edges, in pine forests and in populated areas [68]; the plant is toxic to most species of productive animals. The active spread of this species in recent years has been facilitated by an increase in the area of fallow land, increased nitrogen levels in the air, targeted planting in roadside green spaces, and climate changes such as drought [69]. This has led to increased plant populations in pastures and grasslands, resulting in hay contamination [70]. Horses are particularly sensitive to the plant's toxic effects and generally avoid this weed, but poisoning can occur when animals graze poorly maintained pastures or when feed such as hay or silage is contaminated [71]. The alkaloids it contains cause liver damage followed by damage to the central nervous system, accompanied by ataxia and secondary photodermatitis [72-74]. The drying reduces the bitter taste of this plant, reducing feed selectivity in horses [75, 76]. An important factor influencing selectivity in horses when consuming feed is the formation in foals during early ontogenesis of feed habits which are based on imitation of the feeding behavior of their mothers [77]. Early diagnosis of poisoning is extremely difficult because many common biochemical and histopathological features of the disease are nonspecific and cannot distinguish poisoning from other immune, infectious or toxic diseases [78]. If liver disease is advanced, the prognosis is generally poor and treatment options are only palliative [79]. Poisoning of animals is accompanied by a number of clinical manifestations. Particularly, horses lose weight, signs of jaundice appear, hyposensitivity to external stimuli is observed (animals often stand with their heads down and may stop chewing feed in the mouth), tremors (especially in the head and neck area), frequent yawning and difficulty swallowing occur which can cause feed to be aspirated (inhaled) or regurgitated through the nasal cavity. Affected horses walk in a straight line or in circles, bumping into objects. Pressing on the head can often cause an animal to have a panic attack and run away uncontrollably. The disease is usually fatal, lasting from a week to several months [80].

Meadow saffron is found in the western and southern regions of Russia, usually growing in damp meadows. All parts of the plant are poisonous, especially the bulbs, since they contain the highly toxic tropolone alkaloid colchicine, which causes intractable multiple organ failure [81]. Colchicine is mutagenic and has the greatest effect on cell division and inhibition of tubulin polymerization, preventing spindle formation during mitosis. The main targets are organs with high mitotic potential, including the gastrointestinal tract, liver and kidneys [82]. Clinical signs develop approximately 48 h after ingestion and typically include drooling, dysphagia, colic, diarrhea, and malodorous stool with tenesmus, and may also include a history of bloody urine and cough [83]. In Germany, a case of horse poisoning

was recorded after feeding a batch of hay heavily contaminated with meadow saffron (apprx. 1.48% of the total mass). Three out of 17 horses developed colic; after a few days, one animal died; at autopsy, intense accumulation of serous or serous-hemorrhagic fluid was noted in the chest and abdominal cavity [84]. One study found that horses can consume contaminated hay when provided with free access to good quality hay [85].

Plants containing neurotoxins. Plant metabolites that have a neurotoxic effect have different chemical natures and specific mechanisms of action on the body, which underlie pathological changes caused by shifts in biochemical processes. One such compound is the unsaturated aliphatic alcohol cicutoxin, extracted from Cicuta species, which targets biomembranes that control the import and export of metabolites and ions in cells [86, 87]. Cicutoxin blocks Na^+ and K^+ channels and has a cholinergic effect on the central nervous system by acting as a noncompetitive antagonist of gamma-aminobutyric acid that binds to the beta domain of its receptor. This deactivates the receptor and disrupts the flow of chloride ions across the membrane, leading to unrelenting neuronal depolarization. Excessive stimulation of motor neurons leads to generalized seizures, resulting in death from respiratory failure [88]. At autopsy, lesions of the cardiac and skeletal muscles are observed, which are limited to pale areas, while multifocal degeneration of the myocardium is noted due to necrosis of myofibrils and replacement fibrosis in the tissues of the heart. Depending on the severity of convulsions, serum concentrations of lactate dehydrogenase, aspartate aminotransferase, and creatine kinase increase [89].

Neurotoxic effects have also been observed when horses consume plants containing the enzyme thiaminase I, which breaks down vitamin B_1 (thiamine), which plays an important role in the metabolism of carbohydrates, fats and proteins, and acts as a cofactor in enzymatic pathways responsible for energy production. Thiamine is an important cofactor in the decarboxylation of pyruvate to acetyl-CoA, which subsequently enters the tricarboxylic acid cycle. Deficiency of this vitamin impairs cellular energy processes and limits certain metabolic pathways, leading to systemic accumulation of pyruvate and lactate and, as a result, cerebrocortical necrosis (polioencephalomalacia) due to neuronal degeneration and death [90].

The poisonous plant *Cicuta virosa* L. of the *Apiaceae* family is one of the most toxic plants in the world. The range of this species includes the northern border of the forest zone. *C. virosa* grows in all regions of the European Russia, in Siberia and the Far East, rarely in Central Asia and the Caucasus, in swamps, damp meadows, marshy banks of rivers and lakes [91]. All parts of the plant contain cicutoxin, its toxicity decreases throughout the growing season, but the roots remain highly toxic all year round. Cicutoxin is not destroyed by high temperature and long-term storage. Poisoning most often results from grazing animals on pastures with depleted grass, in places where this species grows abundantly, as well as uncontrolled movement of animals. Additional factors contributing to the consumption of this plant are hunger and fatigue of animals, as well as their need for green food after the winter diet. In most cases, poisoning occurs at the early stage of the plant's growing season, when horses, tearing off young leaves and stems, remove the plant along with the rhizome from the soft, damp soil and eat it. In horses, severe poisoning occurs if they eat 1-2 rhizomes or 200-250 g of plant mass. Clinical gastrointestinal symptoms of poisoning include increased salivation and colic, cardiovascular and respiratory symptoms are tachycardia (rapid heartbeat) and tachypnea (rapid breathing). The animal becomes fearful, excited, coordination is impaired, and muscle tremors occur. Within 15 min of the first symptoms appearing, the horse may collapse [92].

Equisetum arvense L. is distributed throughout Russia everywhere except deserts, semi-deserts and the Far North. It prefers poorly drained sandy, fairly rich, moderately moist soils, and therefore is found in forests, upland and floodplain meadows, the edges of swamps, pebbles, sandbanks, fields, pastures, along the banks of rivers and streams [93]. It can seriously suppress field crops and other plants, and therefore often alone or together with cereals dominates the grass cover of water meadows and fallow lands. *Pteridium aquilinum* (L.) Kuhn. grows in coniferous and deciduous forests of the European Russia, Siberia, the Far East and the Urals. It is found on forest edges, open hills and in thickets of bushes, preferring light and poor soils, often dominating the grass cover. These plants contain the enzyme thiaminase, which catalyzes the hydrolysis of vitamin B_1 (thiamine) produced by microbial synthesis in the intestinal tract of horses, thereby causing deficiency [94]. The clinical signs of poisoning reflects the state of vitamin (thiamine) deficiency. Symptoms begin slowly and the first signs may include a general unkempt appearance, weight loss (without significant loss of appetite), diarrhea and slightly uncoordinated movements. If the animal is left untreated, the disease progresses to the point where the horse loses muscle control, has an unsteady gait, and has severe balance problems. The horse becomes restless, may lie down and be unable to get up, and convulsions occur. Ultimately, the animal may die from exhaustion within approximately 1-2 weeks [95-97]. *P. aquilинum* also contains the toxin ptaquiloside, found in the highest concentrations in young growing parts of the plant, which is thought to be responsible for bone marrow suppression and carcinogenic activity [98, 99].

Plants containing photosensitizing substances. Some plant species, such as buckwheat (*Fagopyrum esculentum* Moench) and St. John's wort (*Hypericum perforatum* L.), are capable of accumulating various biologically active substances, e.g., hypericin, fagopyrin, phyloerythrin, furocoumarin, etc., which, when ingested by animals, cause primary photosensitization, or light-induced photodermatitis of exogenous origin [100]. Possessing fluorescent and resonant properties, these substances become phototoxic when exposed to ultraviolet radiation. Clinical signs of photosensitivity dermatitis usually develop within a few hours of exposure to sunlight. Photodynamic agents, or chromophores, are absorbed into the gastrointestinal tract and transported through the circulatory system to organs and tissues. Hair and skin pigments have protective properties because they absorb light energy before it activates chromophores and damages skin tissue. The photosensitizing effect of these substances causes an increase in the sensitivity of non-pigmented areas of the skin, visible mucous membranes and eyes of horses to ultraviolet radiation, since its exposure activates the accumulation of toxic compounds. This initiates a destructive cascade of chemical reactions against susceptible substrates within cells (e.g., lysosomes, mitochondria, cell membranes, lipids, proteins, nucleic acids) and resulted in localized foci of inflammation [101].

Photodynamic substances are activated by photons and converted into high-energy compounds that cause tissue damage by releasing inflammatory mediators and producing free radicals, also known as reactive oxygen species. These are highly reactive molecules that damage membranes, disrupting cell permeability and homeostasis, leading to cell death [102]. As a result, inflammatory reactions develop in non-pigmented areas of the skin, which are accompanied by redness (erythema), swelling, itching and peeling [103, 104]. Large lesions may progress to blistering, ulceration, exudation, skin necrosis, and sloughing of necrotic tissue, which may lead to secondary bacterial infection. In horses, the most severely affected areas are poorly pigmented areas that are not well protected by the coat and exposed to the sun, especially the face, ears, eyelids, vulva and coronary bands; the tongue and oral cavity may also be affected. In severe cases of the

disease, photosensitivity can develop even in animals with dark and thick hair. Photophobia is also a clinical feature of the disease [105].

St. John's wort is widespread in Eurasia, often growing as a weed in forests, abandoned fields and pastures, along roads and reservoirs, and is poisonous at all stages of growth. In the spring, horses are attracted to young, tender shoots, and hay contaminated with them can cause poisoning in the winter [106]. Cases of photodynamic dermatitis have been reported in the Czech Republic when horses grazing on pastures contaminated with St. John's wort [107, 108].

Buckwheat is a plant widely cultivated in southern and central Russia, which is often used as a precursor that has a beneficial effect on biological processes in the soil, improving its physical, mechanical, agrochemical properties and phytosanitary condition. Occasionally it is found as a weedy alien plant in crops and along roads [109].

Sporadic cases of outbreaks of primary photosensitivity have been reported in horses fed predominantly alfalfa hay [110].

Plants containing cyanogenic glycosides. Apprpximtely 2,600 plant species contain cyanogenic glycosides which are a potential cause of acute and chronic poisoning in animals. Cyanogenic glycosides most often belong to monoglycosides (durrin, prunasin, linamarin, lotaustralin), their main carbohydrate component is D-glucose, and the cyanohydrin part is stabilized by a β-glycosidic bond. The most dangerous plants for horses are Sudan grass *Sorghum sudanense* (Pers.) Stapf and black elderberry *Sambucus nigra* L. [111]. By the enzymatic hydrolysis of cyanogenic glycosides in the gastrointestinal tract, a highly toxic compound, the hydrogen cyanide is formed which binds to the ferric iron of the cytochrome oxidase of the mitochondrial respiratory complex and forms the cyanide-cytochrome oxidase complex. As a result, the transport of electrons to molecular oxygen stops, the entire respiratory chain is blocked, which leads to cellular hypoxia, or cytotoxic anoxia. Because of the high content of hemoglobin saturated with oxygen and due to disruption of the process of oxygen absorption by tissues, the color of venous blood becomes bright red. In addition to cytochrome oxidase, in mammals, the activity of at least 40 enzyme (lactate dehydrogenase, catalase, peroxidases, etc.) is inhibited. Simultaneously with inhibition of the electron transport chain, the ATP synthesis, which is necessary to ensure biochemical processes in cells, is disrupted [112].

Clinical signs appear very quickly after animals consume large amounts of cyanogenic plants. In acute cyanide poisoning, death occurs within a period of several minutes to several hours. Animals exhibit signs of agitation and generalized muscle spasms, an unsteady gait, followed by severe clonic convulsions, as well as respiratory distress (shortness of breath), which develops as a compensatory response to tissue hypoxia, that is, the frequency and depth of respiratory movements increase. There is also lacrimation and drooling, mydriasis (dilated pupils) and bright color of the mucous membranes [113].

When small amounts of toxins are consumed within a few weeks, clinical symptoms associated with spinal cord and nerve damage begin to appear due to the destruction of the myelin sheath of peripheral nerves. Horses, due to impaired proprioceptive function, gradually develop ataxia (disorder of motor coordination), which is most noticeable when the animal is asked to turn. As the disease progresses, paralysis of the tail and hind limbs may occur. Due to damage to the nerves innervating the bladder, animals develop equine cystitis-ataxia syndrome, accompanied by incontinence (urinary incontinence) which in females leads to burns of the hind legs and, in some cases, to inflammation of the bladder and kidneys. In pregnant mares, toxins can cause abortion or cause skeletal malformations in the developing fetus. Once neurological symptoms appear, nerve

damage is irreversible and the prognosis for the animal is poor [114].

Sudan grass is a valuable forage pasture and hay crop. On the territory of Russia, it is cultivated in the southern and southeastern regions of the European part, in the Altai Territory and in the Far East. Sudangrass toxicity is associated with the formation of free hydrocyanic acid in the plant after drought or frost [115]. Cyanides are present in the form of glycosides mainly in the leaves and seeds and only in trace amounts in the stems. Hay is generally safe because the glycosides are hydrolyzed during storage [116, 117].

Black elderberry grows in the south of the European Russia, as an undergrowth in coniferous and deciduous forests, easily runs wild and spreads along roads, in populated areas and in wastelands. All parts of the plant are poisonous, with the exception of flowers, shell and pulp of ripe berries [118].

Plants containing cardiac glycosides. Many plants of different families synthesize toxins that directly or indirectly affect the functioning of the cardiovascular system. So-called cardiotoxic plants contain cardiac glycosides (gitoxin, digoxin, convallamarin, etc.), which cause acute pathological processes and sudden death of horses [119]. Species containing cardiac glycosides grow on the territory of Russia, among which the most dangerous for horses are *Convallaria majais* L., oleander *Nerium oleander* L. and representatives of the genus *Digitalis* L. [120].

Cardiac glycosides inhibit adenosine triphosphatase in cell membranes, causing electrical conduction disturbances in the heart muscle [121]. They inhibit the active transport of Ca^{2+} and K^{+} ions across plasma membranes, which increases the amount of Ca^{2+} inside cardiomyocytes, leading to cell death and secondary arrhythmias [122, 123] due to disruption of Hiss bundle conduction. Cardiac lesions are the main diagnostic marker of oleander poisoning in horses [124]. Animals experience short-term bradycardia, then the heart rate increases and arrhythmias appear. Glycosides have a local irritant effect on the gastrointestinal mucosa, and therefore clinical symptoms include hypersalivation and colic. Glycosides also take part in the development of pathological processes in the respiratory system, slowing down its functioning, which is clinically expressed by difficulty breathing. There is an increased release of exudate, an inflammatory process develops, accompanied by an increase in the number of opportunistic microflora, which contributes to secondary intoxication and leads to the appearance of muscle tremors, ataxia and the inability of the animal to stand. In addition, an irregular and weak pulse due to decreased cardiac output leads to hypothermia of the limbs, and the animal often experiences clonic convulsions before death [125]. Cardiac glycosides can pass into mother's milk and pose a risk to foals [126].

C. majais is a herbaceous plant growing in the European Russia, in Transbaikalia, the Amur region, Primorye, Sakhalin and the Kuril Islands [127]. All parts of the plant are toxic, with the highest concentration of cardiac glycosides in the roots. The plant also contains various saponins. *C. majais* is considered one of the most potent cardiotoxic plants as more than 38 cardiac glycosides have been identified in it, including convallatoxin, convallarin, and convallamarine [128].

Oleander is an evergreen ornamental shrub, common on the southern coast of Crimea, the Black Sea coast of the Caucasus and in Transcaucasia [129]. All parts of the plant, both fresh and dried, are poisonous and contain varying amounts of cardiac glycosides, especially oleandrin. The toxicity of oleander varies depending on the color of the flower and the time of year. Fatal intoxication for most mammals is possible with consumption of the plant in amounts as low as 0.005% of the animal's body weight [130, 131]. The plant also contains saponins and terpenoids. Although horses rarely eat green oleander leaves because they are unpalatable, there is a possibility that dried leaves accumulate in long-grass

pastures or end up in a horse's daily diet and may be ingested by the animal. Horses ingesting a lethal dose of oleander leaves are often found dead within 8-10 h, and symptoms of poisoning rarely last more than 24 h before death [132].

Digitalis is a genus of herbaceous plants containing the cardiac glycoside digoxin. On the territory of Russia, foxglove species grow in the Caucasus, in the European part and Western Siberia, in meadows, deciduous and mixed forests [133]. All parts of the plant are poisonous; the toxic dose for horses can be several hundred grams of the fresh plant, and when dried, this amount is significantly reduced [134].

In summary, poisoning of horses by poisonous plants is a relatively common phenomenon worldwide, causing serious economic harm to animal owners [135-138]. The main reason for horse consumption of these plants is the lack of control over the botanical composition of pastures and hayfields, which is especially important in the context of the spread of invasive species [138]. Clinical signs of plant poisoning in horses range from mild distress to sudden death, and diagnosis can rarely be made based on the clinical syndrome alone [139, 140]. Accurate diagnosis usually requires a history of exposure to the plant, making accurate identification necessary.

So, phytotoxins from poisonous plants are substances diverse in structure and mechanism of action on the body. The most common plants in Russia that are dangerous for horses contain alkaloids, neurotoxins, photosensitizing substances, cyanogenic and cardiac glycosides. Plant species containing different groups of alkaloids include bindweed, aconite, meadow saffron, henbane, datura, spotted hemlock and meadow groundsel. Pyrrolizidine alkaloids are hepatotoxic, and horses may experience secondary photosensitization when exposed to sunlight. Tropane alkaloids have an anticholinergic effect, acting as an inhibitor of the neurotransmitter acetylcholine. Piperidine alkaloids are toxic to adult horses and cause teratogenic effects. A neurotoxic effect is exerted by cicutoxin contained in the poisonous stem, as well as thiaminase produced by horsetail and bracken. The development of primary photosensitivity in horses is observed when consuming buckwheat and St. John's wort. Sudan grass and black elderberry contain cyanogenic glycosides which cause cellular hypoxia and disrupt the activity of the central and peripheral nervous system. Convallaria, oleander and foxgloves synthesize cardiotoxic substances that disrupt the functioning of the cardiovascular system of horses. Since there is no antidote for most toxins found in poisonous plants, treatment of poisoning is primarily symptomatic and supportive. In this regard, the best measure to combat phytotoxicoses should be considered prevention, which should first include a thorough check of hay and silage, and the removal of toxic plants from pastures.

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