



REVIEW ARTICLE

A Review on the Applications of Potassium Permanganate in Veterinary Medicine: Toxicity, Efficacy and Future Considerations

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ABSTRACT

Potassium permanganate (KMnO₄) solution, a potent oxidizing agent, has been extensively employed in veterinary medicine for uterine washing, wound cleansing, and many other therapeutic purposes. However, its related toxicity and adverse effects often remain unnoticed due to its extensive use as an antiseptic and disinfectant. This review aims to explore the potential risks and harmful effects of using potassium permanganate in veterinary medicine. Through an in-depth review of the scientific literature and authoritative analysis, this article discusses the significance of various antiseptics, the mode of action of potassium permanganate, its pharmacokinetics, dosage, toxicity, allergenicity and historical use in the human and veterinary practices. As a vital constituent of numerous commercially important chemical entities, including medicines, potassium permanganate is used for wound cleansing and uterine flushing because it can effectively disrupt cell wall and damage DNA of pathogenic organisms, effectively mitigating bacterial and fungal infections. However, it can also adversely affect living cells, leading to inflammation, oxidative stress, and ulcerative injury. Excessive and prolonged exposure of body tissue to potassium permanganate can cause damage to vital organs such as the liver and kidneys, induce digestive system malfunctions and provoke reproductive disorders. Furthermore, it can contaminate milk and meat, and potentially instigate a reduction in milk production of the animal. The present review primarily aims to enhance veterinarians' understanding regarding the therapeutic applications and potential hazards of KMnO₄, as well as to highlight the importance of its judicious use to minimize its negative repercussions on animal and human health.

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INTRODUCTION

Potassium permanganate, also known as KMnO₄, is a chemical compound of manganese (Mn) with significant economic value (França *et al.*, 2013). It serves as a potent oxidizing agent in an acidic medium but exhibits weaker activity in basic media (Palaniappan and Karthikeyan, 2022). Additionally, it forms a brown MnO₂ crystal precipitate under neutral pH (Shefer *et al.*, 2002).

Potassium permanganate appears as dark, odorless, purple crystals that yield pink to deep purple solutions in water based on its concentration (Palaniappan and Karthikeyan, 2022). As a topical antiseptic and disinfectant, it is used in wound cleansing and vaginal douching (Fig. 1). However, it is hazardous if ingested and can cause irritation in the mucous membranes (França *et al.*, 2013; Subramanya *et al.*, 2018). Upon contact with organic matter, it generates nascent oxygen and forms manganese dioxide

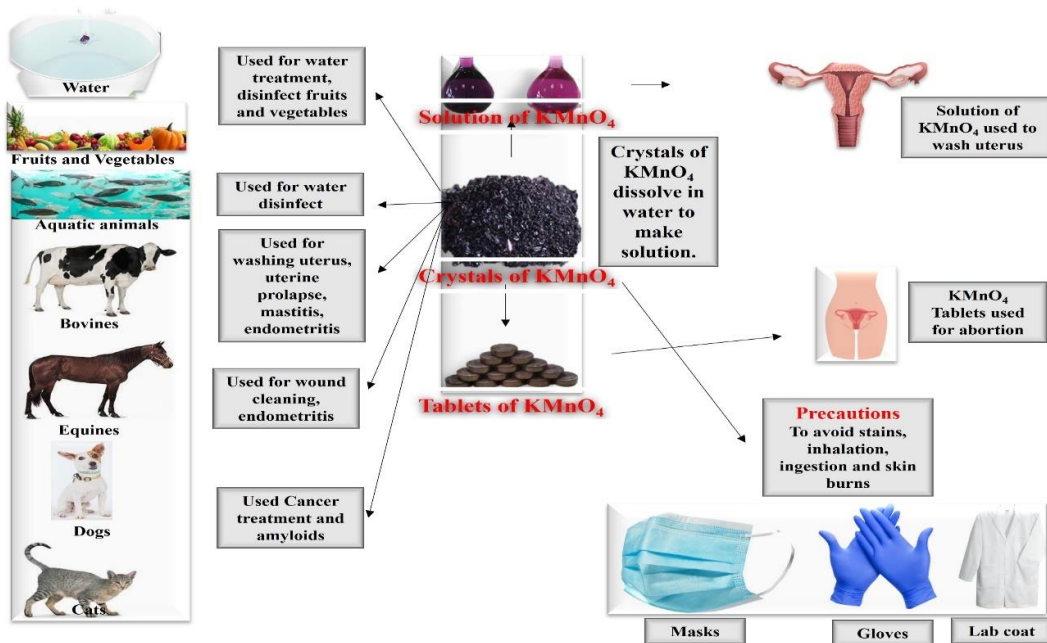
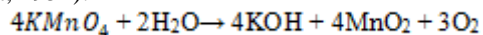


Fig. 1: Overview of potassium permanganate and its applications.

(Dash *et al.*, 2018). At low concentrations, it merely causes irritation. However, at higher concentrations, due to the production of potassium hydroxide, it can lead to more severe damage because it can permeate deeper into tissues, as represented by the following reaction (Lammert and Scott, 1954):



However, despite its widespread availability in the market, its toxic effects often go unrecognized. For instance, ingesting KMnO₄ may result in substantial toxicity, potentially leading to severe morbidity and mortality (Korkut *et al.*, 2013). It has numerous applications, including medical therapy, industrial wastewater treatment, as a chemical reagent in laboratory settings and in the preservation of fruit and vegetables (Chen and Yeh, 2005; Wattanathorn *et al.*, 2018). The severity of the effect of KMnO₄ is contingent upon its concentration, exposure duration and route of administration. Most of the organs damage is attributed to ingesting and inhaling KMnO₄, causing hemorrhage, edema, upper gastrointestinal tract damage and respiratory difficulties (Özyiğit *et al.*, 2020). Both communities and hospitals have been using potassium permanganate for topical treatment, vaginal douching and uterine washing since long (Ebadian *et al.*, 2022). This is predominantly due to the ability of this compound to disrupt the DNA structure and alter the cell walls of pathogenic bacteria, viruses and fungi. Additionally, it promotes the production of collagen and granulation tissue which are essential factors in the healing process (Fan *et al.*, 2013; Brandt *et al.*, 2016).

Historically, potassium permanganate solution has been used for vaginal douching and tablets for inducing abortions (Brudenell, 1961). However, due to its toxic effects, safety and illegal use, its application in human medicine is not recommended, predominantly for topical applications. In veterinary medicine, the usage of potassium permanganate remains widespread in Asia. Despite its long history, sufficient evidence supporting its efficacy in treating oozing wounds is lacking, rendering its medicinal use controversial. It is most frequently

applied for uterine washing in cows for the treatment of conditions such as uterine prolapse, endometritis and teat dipping in cases of mastitis. In dogs and cats, it is used for the treatment of mammary cancer (Yano *et al.*, 1981; Rowland *et al.*, 1991; Delgado-Enciso *et al.*, 2018; Abdulla *et al.*, 2020).

Nevertheless, there is a lack of research concerning the toxic effects of potassium permanganate solution in bovine uterine washing. In this article, given the medical significance of potassium permanganate, we aimed to gather data to evaluate whether potassium permanganate offers more therapeutic benefits than adverse effects in veterinary medicine.

Review methodology: A comprehensive topic analysis was conducted, drawing upon various scientific journals, research studies and authoritative websites. Relevant research studies were identified through electronic databases such as PubMed, Google Scholar and Science Direct. Studies were selected based on their pertinence to the topic and their scientific rigor. Additionally, authoritative sources, including veterinary textbooks and government agency reports, were also consulted.

Significance of various antiseptics: Increasing resistance to systemic and topical antibiotics has been observed over time (Ousey and McIntosh 2009). Antiseptics have been used as a potential alternative to antibiotics for treating topical wounds, demonstrating broad-spectrum antimicrobial activity and superior microbicidal properties compared to many antibiotics (Lachapelle *et al.*, 2013). Furthermore, antiseptics present multiple mechanisms of action against targeted microbes, reducing the likelihood of resistance development compared to antibiotics (Leaper *et al.*, 2012). Given the availability of suitable antiseptics, topical antibiotics are not recommended. Furthermore, the World Health Organization has issued guidelines promoting the use of antiseptics to prevent systemic antibiotic usage (WHO, 2018). Ideally, an effective antiseptic should possess several favorable properties, including high penetration ability into biofilms, eschar,

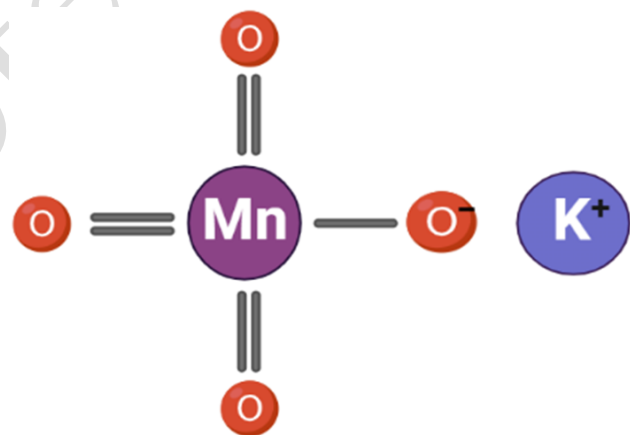
Table 1: Characteristics and applications of commonly used antiseptics

Antiseptic name	Mode of action	Spectrum	Applications
Alcohols (Sebben, 1988; Dumville <i>et al.</i> , 2013)	Reduces cell membrane surface tension, denatures proteins, destroys cell membranes	Exhibits bactericidal action against gram-positive and gram-negative bacteria, mycobacteria, fungi, and lipid-enveloped viruses	Primarily used to clean wounds, not for surface rubbing.
Iodinated compounds (Iodine; Iodophors) (Goldenheim, 1993; Dörfel <i>et al.</i> , 2021)	Precipitates bacterial proteins and nucleic acids, alters cell membranes, interferes with respiratory chain by blocking electron transport through electrolytic reactions with enzymes	Active against gram-positive and gram-negative bacteria, mycobacteria, fungi, and enveloped and non-enveloped viruses	Used for wound cleaning, uterine washing, and post-surgery application
Chlorhexidine (Hibbard, 2005; Stahl <i>et al.</i> , 2007)	Passively diffuses through bacterial membranes, alters membrane permeability, and inhibits enzymes in periplasmic space.	Strongly active against gram-positive bacteria; inhibits enveloped viruses	Antiseptic for skin, erosions, superficial wounds, and minor burns
Triclosan (Chuanchuen <i>et al.</i> , 2001)	Penetrates bacterial cells, altering the cell membrane and the synthesis of RNA, fatty acids, and proteins	More active against gram-positive bacteria than gram-negative bacteria, also active against mycobacteria and yeast	The main application is for hand washing.
Surfactants (Soaps, derivatives of ammonia) (Klimaszewska <i>et al.</i> , 2022)	Inactivates enzymes and denatures proteins of cytoplasm for microorganisms	Bactericidal effects more pronounced for gram-positive bacteria than gram-negative bacteria	Used as antiseptics in hand hygiene in alcohol-based formulations
Hydrogen peroxide (Urban <i>et al.</i> , 2019)	Produces hydroxyl and free radicals that attack the essential components of microorganism structure	Active against bacteria (especially gram-negative and anaerobes), fungi and some viruses	Used as an antiseptic, disinfectant and sterilant
Heavy metal derivatives (Silver salts, mercury) (Türker <i>et al.</i> , 2022)	Causes bacterial wall breakage, binds to bacterial DNA, interferes with cell division and replication	Bacteriostatic against gram-positive and gram-negative bacteria; act against fungi	Used for prevention and treatment of 2 nd and 3 rd -degree burns
Ethacridine lactate (Adaydin <i>et al.</i> , 2019; Ziętek <i>et al.</i> , 2020)	Suppression of microbial protein synthesis, attaches itself to bacterial DNA and prevents the organism from synthesizing DNA and RNA.	Bactericidal against gram-positive, gram-negative bacteria and pathogenic fungi.	Used to treat wounds, mucous membrane infections and purulent skin infections

and necrotic tissue, broad-spectrum activity, low potential for acquired resistance, high local tolerability, and wound healing ability by mitigating inflammation (König *et al.*, 1997; Lipsky and Hoey, 2009; Leaper *et al.*, 2012). During wound care, the prevention or treatment of infection can be performed by selecting suitable antiseptics. Different antiseptics include alcohols, iodinated compounds, chlorhexidine, triclosan, surfactants, hydrogen peroxide and heavy metals (Table 1).

Potassium permanganate (KMnO₄): Potassium permanganate was discovered in 1959 by Johann Rudolf Glauber, a German-Dutch chemist (Glauber, 1959). This water-soluble compound is composed of two ions: potassium and manganite (Fig. 2). Due to its potent oxidizing properties, potassium permanganate serves as an exceptional disinfecting and deodorizing agent, and it is not inherently toxic (Cheng and Chai, 2010). Moreover, potassium permanganate displays astringent characteristics. In cases of acute dermatoses and eczematous conditions, particularly when a secondary infection is present, a solution of KMnO₄ is administered.

Furthermore, potassium permanganate can be used as a cleaning agent for wounds, ulcers, or abscesses and in the preparation of moist dressings and baths (Hu *et al.*, 2015). Although it displays bactericidal activity *in vitro*, the therapeutic use of this compound as a bactericide is limited due to its rapid degradation in the presence of body fluids. It is typically prepared as a concentrated 0.1% solution in water and then diluted to yield a 0.01% (1 in 10,000) solution. Such solutions have been applied in treating bromhidrosis and mycotic conditions, such as athlete's foot and poison ivy dermatitis (Cheng and Chai, 2010; Mackeen *et al.*, 2015).

**Fig. 2:** Chemical structure of potassium permanganate (KMnO₄).

Potassium permanganate, particularly in its concentrated form, is highly irritating to human skin and eyes. It is combustible and can react vigorously with organic materials or reducing agents (Echols *et al.*, 2015). The antibacterial action of KMnO₄ is exerted through oxidizing the tissues or proteins of bacteria. The external use of KMnO₄ is limited due to the staining of skin or tissues and its destructive oxidation process on all organic matters. In cases of poisoning, such as with chloral hydrate, barbiturates, and alkaloids, KMnO₄ can serve as an antidote via gastric lavage at 1:5000 ratio, inhibiting the absorption of poison and promoting the oxidation of the poison. Extreme caution is necessary during handling because KMnO₄ can cause explosions when it reacts with highly oxidizable substances. Thus, it is stored in tightly sealed containers (Rai, 2020).

Mode of action of KMnO_4 : Potassium permanganate exerts its antimicrobial effects through the reduction of exudation and the coagulation of proteins. This compound disrupts the cell wall and interferes with the DNA of pathogenic microbial organisms, including bacteria, viruses, fungi and protozoa (Fig. 3). It mitigates pruritis and inflammation, decreases vasodilation and removes debris, dirt, scales, and crusts. Furthermore, it stimulates collagen synthesis and granulation tissue formation and exhibits deodorizing action (Majtan, 2011; Fan *et al.*, 2013).

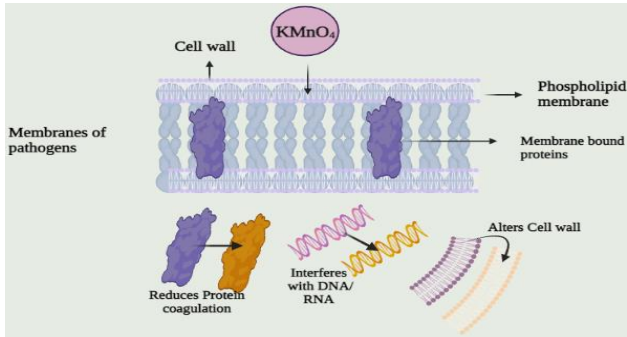


Fig. 3: Showing mechanism of action of KMnO_4 .

Pharmacokinetics of KMnO_4 : Pharmacokinetics, by definition, refers to the process by which the body absorbs, distributes, metabolizes, and eliminates a drug. The KMnO_4 is available in solution, crystal, and powder forms. Upon ingestion, it enters the gastrointestinal tract, is absorbed, and distributed throughout the body, and can induce tingling pain, abdominal pain, diarrhea, vomiting, nausea, shock, or collapse. Inhalation of KMnO_4 may lead to shortness of breath, labored breathing, dyspnea, sore throat, and cough. Direct skin contact with this compound can result in skin burns, redness, and pain. As a solution, it is utilized for uterine and wound washing. High concentrations can induce burning and skin damage and, when applied to the uterus, may cause hemorrhages, oxidative stress, inflammation, and bleeding (De-Méo *et al.*, 1991; Hinderling, 2016). The body does not metabolize potassium permanganate. As an oxidizing agent, its main function is to participate in redox reactions instead of passing through metabolic processes directly. Urine is the main excretory channel for potassium permanganate. Renal excretion is the process by which it is filtered by the kidneys and eliminated as urine. Only a small amount might also be excreted by other means, like perspiration and feces. Due to a lack of pharmacokinetic data, the elimination of half-life of potassium permanganate in humans is not well established. In general, potassium permanganate is not commonly employed as a pharmacological agent in the conventional sense, and there hasn't been much research done on its pharmacokinetics in humans. Its use is primarily restricted to topical applications and water treatment; consuming or inhaling is uncommon and is frequently linked to toxicity rather than therapeutic advantage. Because of this, care should be taken when handling potassium permanganate because of its possible side effects and insufficient pharmacokinetic knowledge (U.S. National Library of Medicine, 2008; WHO, 2004). Adverse effects of the use of KMnO_4 are summarized in Table 2.

Dosages, tolerability, toxicity and allergenicity of KMnO_4 : Potassium permanganate solutions of varying concentrations, including ratios of 1:1000, 1:4000 to 1:10,000, and percentages of 5.0, 1.0 and 0.01 have been used as wound and mouth lotions. They have also been used for douching, irrigating cavities, washing the urethra, and serving as an effective astringent, algicide, and virucide (Abdulla *et al.*, 2020; Wang *et al.*, 2021). Higher concentrations can induce tissue irritation, burning, and blistering in tissues (Martin and McFerran, 2014). Due to its potent algicidal and virucidal properties, KMnO_4 is also utilized for water disinfection, although high concentrations may pollute the water and induce prodromal signs. The primary lesions are hemorrhage and necrosis of the crop in birds (Wang *et al.*, 2021).

To test the short-term toxicity of KMnO_4 , Saganuwan *et al.* (2008) administered different doses of KMnO_4 to Swiss albino mice and monitored their blood and biochemical parameters. The results showed non-significant effects, except that the chloride ion level in the plasma was significantly reduced. Toxicity signs were rapid and shallow respiration, rough hair coat, dullness, diarrhea, bloating, gastroenteritis, congestion of the liver, paleness of the lungs and hypochloremia. According to another study, to determine the toxicity of KMnO_4 , Swiss albino mice were administered KMnO_4 and exposed to *H. sabdariffa* flowers and *M. parviflora* leaves. The results showed severe histopathological changes in the kidney and the liver of Swiss albino mice treated with KMnO_4 , while the treatment with flowers and leaves prevented the damage and exhibited a protective role (Farhan and Mohammed, 2020).

Applications of KMnO_4 in humans: Potassium permanganate has been used for years across various medical specialties, notably dermatology, urology, gynecology, surgery, and internal medicine. While many of these uses have become obsolete, it has been primarily prescribed in dermatology for dermatomycoses, in urology for urethral and bladder flushing, in gynecology as a douche for treating infections of the vagina and pelvic organs, in surgery as a preoperative skin disinfectant, and in medicine as an antidote for certain ingested organic poisons (Philipp, 1953; Marsh and Webster, 1954). Historically, due to its antiseptic properties, KMnO_4 was used for vaginal douching in Europe and elsewhere at concentrations between 0.01 and 1%. The introduction of high concentrations of potassium permanganate into the vagina has been reported to cause vaginal bleeding (Cabaniss and Clark, 1961). A focus on the relative frequency of occurrence and clinical characteristics has been observed. There has been a rise in use of potassium permanganate tablets as abortifacients among American women. Potential adverse effects including uterine damage and bleeding, burned vaginal lesion and a tightly closed cervix are noteworthy. Its ineffectiveness was demonstrated by the fact that none of the women who took this chemical as an abortifacient reported experiencing miscarriage (Philipp, 1953).

Europeans and South Americans seem to be the primary sources of public trust in the effectiveness of KMnO_4 . An urgency exists to discredit its usage. It was observed that tablets, crystals, or douching of potassium permanganate solution were accountable for instances of

Table 2: Adverse effects of KMnO_4

Site of administration	Adverse effects	Symptoms
Topical use	Irritation of skin and mucous membranes	Redness, burning and itching (Chin <i>et al.</i> , 2022)
Inhalation	Respiratory problems	Coughing, bronchitis, and severe asthma (Agrawal <i>et al.</i> , 2014)
Ingestion	Gastrointestinal problems	Abdominal pain, diarrhea and vomiting (Korkut <i>et al.</i> , 2013)
Solution form	Ulcers, inflammation	Endometrial cancers, oxidative stress, ulceration (Anderson, 2003)

vaginal hemorrhage. Some cases involved severe bleeding, with patients admitted in shock conditions requiring whole blood transfusions (Conti *et al.*, 1993).

Case studies also indicate an increasing popularity of potassium permanganate tablets and douches for vaginal application. There is a growing hope to further discourage its usage for treating gynecological conditions (Jetter and Hunter, 1949). Currently, potassium permanganate is categorically prohibited for vaginal douching and abortion in women; however, its use is still permitted for wound healing.

Research uses of KMnO_4 *in vivo* and *in vitro*: Various methods exist for the application of KMnO_4 , such as a topical agent, disinfectant, antiseptic, douching agent, and irrigation. The KMnO_4 holds significant value in clinical applications. A series of experiments are needed to be conducted to determine the precise dosages and concentrations of KMnO_4 for *in vivo* and *in vitro* use. Multiple studies have underscored the importance of KMnO_4 , such as one that administered splenic cells to pyridoxine-deficient mice, demonstrating that skin graft tolerance can be induced. The authors of this study induced chronic inflammation by administering a 1:40 KMnO_4 solution (Fridas *et al.*, 1994). Other research papers described the response of KMnO_4 oxidation during the maintenance and developmental stages of cyanobacteria (Becker *et al.*, 2000; Swearingen *et al.*, 2016).

Applications of KMnO_4 in veterinary medicine

Aquatic animals: Several studies have demonstrated that potassium permanganate can adversely affect aquatic animals. Allison (1957) showed that prolonged exposure to potassium permanganate can be toxic to rainbow trout, causing respiratory distress and diminished survival rates. Fish can exhibit anemia due to potassium permanganate poisoning. Lowered red blood cell (RBC) counts may result from anemia caused by the suppression of erythropoiesis and hemosynthesis, as well as an increase in the rate of erythrocyte breakdown in hemopoietic organs (Adhikari *et al.*, 2004). These changes underscore the direct impact of potassium permanganate toxicity, exhibiting its capacity to cause the death of red blood cells after only brief exposure to the chemical.

Bovines: Potassium permanganate, as a robust oxidizing agent, plays a critical role in veterinary medicine, particularly in the care and management of bovines. It is employed for wound cleaning, teat dipping and uterine washing (Fig. 4). Research has demonstrated that sustained exposure to excessive amounts of potassium permanganate can induce severe damage to the liver, kidneys and digestive systems in cows (De-Meo *et al.*, 1991). This compound can be absorbed via respiratory and oral pathways, potentially accumulating within the body. This accumulation can trigger oxidative stress, inflammation, and tissue damage, leading to liver and kidney failure. Activity of the digestive system may also be compromised, resulting in decreased feed intake,

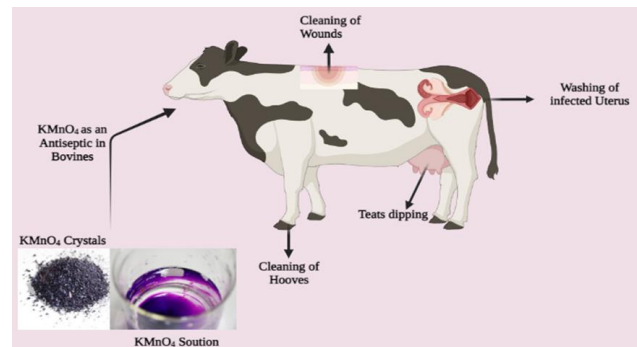


Fig. 4: Showing antiseptic uses of KMnO_4 in bovine

digestive issues, diarrhea, and substantial economic losses for farmers (Karthik *et al.*, 2014; Bigliardi *et al.*, 2017). Potassium permanganate solution is utilized for uterine washing both pre- and post-pregnancy. During pregnancy, harmful effects can occur due to exposure at this crucial stage, potentially leading to abortion, fetal malformation and similar other reproductive complications (Hasan *et al.*, 2017). Various uterine diseases, such as endometritis, metritis and uterine prolapse, require uterine washing with KMnO_4 before treatment (Gupta *et al.*, 2018; Khair *et al.*, 2018).

The most common and traditional method for treating uterine prolapse in cows involves washing the uterus with potassium permanganate. Uterine prolapse typically occurs when the cervix is open and lacks tone, causing the uterus to invert as it passes through the vaginal canal. The prolapsed mass is irrigated with a 1:1000 potassium permanganate solution (Hu *et al.*, 2015). Although potassium permanganate has been used for uterine washing in cows with endometritis, no research evidence supports this treatment. In some countries, a 0.01-2.0% KMnO_4 solution is used for flushing and disinfection purposes, yet it cannot be recommended due to a lack of research evidence (Abinaya and Thangarasu, 2017). Furthermore, potassium permanganate solution is applied as a teat dip for the prevention of mastitis. One study compared the efficacy of a teat protection spray with 1.0% KMnO_4 teat dip solution, indicating a higher efficiency for the teat protection spray (Sukumar *et al.*, 2019). As a vital product of dairy farming, milk demands strict quality control. Contamination of milk with potassium permanganate can negatively affect human health, potentially causing skin irritation, nausea, vomiting, and liver and kidney damage. Therefore, routine milk quality testing is critical for ensuring consumer safety and preventing adverse effects due to KMnO_4 contamination.

Historically, it was claimed that douches containing different chemicals could be used for the treatment of granular vulvo-vaginitis in approximately 30 days. Subsequent findings revealed that creams and powders with bacteriostatic properties were more beneficial (Hunter *et al.*, 1958). In another study, sections of the mink endometrium during delayed implantation, early post-

implantation and pseudopregnancy were fixed in buffered osmium tetroxide with sucrose or potassium permanganate (Enders *et al.*, 1963). In conclusion, there is an imperative need for further research to explore the effects of KMnO_4 solutions in veterinary medicine to substantiate both the advantages and disadvantages of this compound.

Canines, felines, and equines: Vesicular stomatitis is a viral disease characterized by ulceration and vesicles formation on the tongue, oral mucosa, coronary band, and teats. It commonly occurs in horses, cattle, swines and rarely in humans. A 0.5% solution of KMnO_4 was used to wash and clean teats, coronary bands and oral mucosa in vesicular stomatitis (Gallo *et al.*, 1950). The utilization of potassium permanganate for uterine lavage in horses has been associated with adverse effects, mainly when administered in high concentrations.

The application of KMnO_4 in veterinary medicine extends beyond bovines and equines and is also used in the care of canines and felines. The extracellular deposition of amorphous, congophilic protein within tissues, a characteristic feature of several clinical syndromes caused by amyloid, is a common clinical syndrome in canines and felines. Different reports suggest that primary amyloids retain birefringence under polarized light following treatment with potassium permanganate and Congo red staining (Yano *et al.*, 1981). However, high-concentration of KMnO_4 has been associated with harmful effects, particularly for wound cleaning. Furthermore, it has been observed that using KMnO_4 can cause a significant increase in the expression of pro-inflammatory cytokines, indicating an inflammatory response to this compound.

Applications of KMnO_4 in veterinary clinics:

Potassium permanganate has a wide range of applications in veterinary clinics. The most common clinical use of KMnO_4 is for washing uteri in cows. Endometrial inflammation is more commonly seen in cows. Clinically, the main feature is the discharge of brown or white discharge. During the treatment, the uterus is first rinsed with 0.1% potassium permanganate solution, and then 5~10 grams of oxytetracycline powder in 500 mL of normal saline is infused into the uterus, which can show a good therapeutic effect (Yadav *et al.*, 2017).

Foot and mouth disease refers to purulent inflammation of the dermis and stratum corneum tissue of animal hooves and is more common in ruminants, especially cows and buffaloes. When treating hoof rot and mouth lesions, the wound is first washed thoroughly with 1% potassium permanganate and ichthyolite ointment is applied to the swollen area, and then hoof bandage is wrapped or installed with gauze (Pathak *et al.*, 2012; Kass *et al.*, 2022;). In many other diseases such as stomatitis, uterine prolapse and food poisoning, 2% or 0.1% KMnO_4 solution is used for washing. In skin abscesses and ulcers, 0.1% concentration is used for cleaning (Crandell, 1981). These broad uses of KMnO_4 are in practice, but there is limited published data available to support this information.

Other clinical applications of KMnO_4 : The most common clinical use of KMnO_4 is uterine washing in cows. However, KMnO_4 has other applications as well. For instance, in South Africa, KMnO_4 is used in traditional medicine, although studies indicate that it can

cause poisoning. Despite a lack of pharmacopeia and awareness, it remains a commonly used traditional medicine in the region (Street *et al.*, 2018). KMnO_4 has proven effective in treating certain types of wounds. KMnO_4 was once thought to be a snake venom antidote. The process of neutralizing snake venom involved injecting potassium permanganate subcutaneously (Gomes, 2012). One study demonstrated the therapeutic value of KMnO_4 in diabetic foot ulcers, showing that a 5% KMnO_4 solution, coupled with standard treatment, enhanced the healing process of these ulcers (Delgado-Enciso *et al.*, 2018). Other studies showed that in the early stages of infection with *F. columnaris*, use of KMnO_4 is beneficial therapeutically, but its benefits are restricted as the infection worsens. The assessment of the level of oxidative stress using various dosages of KMnO_4 and the impact of antioxidants at different concentrations of vitamin C on female infertility demonstrated the role of oxidative stress in female infertility. These findings supported the advantages of using antioxidants in treating this illness to enhance the follicular environment and modify the hormonal profile associated with female infertility. The KMnO_4 can also induce chronic inflammation at a dose of 200 μL with a concentration of 1:40 in mice (Darwish *et al.*, 2009).

Adjunctive uses of KMnO_4 in clinical therapy:

Synergistic drug interactions occur when the combined effect of two or more drugs exceeds the sum of their individual effects. In the context of uterine prolapse, KMnO_4 is utilized for uterine washing in conjunction with dextrose and sodium chloride (DNS) 5%, calcium borogluconate and drotaverine hydrochloride (Kumar, 2014).

In another study examining the oxidative stress of KMnO_4 , various dosages of the compound were administered in conjunction with Vitamin C. The results revealed that the combined KMnO_4 and Vitamin C demonstrated higher efficacy than either the KMnO_4 or Vitamin C alone. For treating diabetic foot ulcers, a 5% KMnO_4 solution was applied daily in addition to typical treatment. After 21 days, the KMnO_4 group exhibited a higher recovery than the standard treatment group (Al-Katib *et al.*, 2012). In bovines, KMnO_4 solution is used along-with antibiotics and hormonal therapy for treating endometritis (Kumar *et al.*, 2015). These studies have proven that KMnO_4 has a more beneficial effect when used synergistically. Therefore, it is plausible that KMnO_4 may be utilized as a synergistic drug in the future.

Precautions in the use of KMnO_4 : Potassium permanganate, a purple oxidizing reagent, can cause staining. To avoid this, certain precautions should be taken before its use, such as wearing proper gloves and an apron to prevent skin burning and staining. It is stable under normal conditions, but if it comes in contact with incompatible materials such as acids, peroxides and reducing agents, it can cause an explosion. A mask should be worn to prevent ingestion and inhalation, and tablet forms should be avoided. Higher concentrations or dosages of KMnO_4 should not be used.

Future perspectives and conclusion: The broad antiseptic and disinfectant properties of potassium

permanganate cannot be denied. However, there is limited published evidence on the effectiveness of potassium permanganate for washing and irrigating the uterus in bovines, such as in treating postpartum infections and uterine prolapse in cows and buffaloes. There is also a need for more research to determine the exact concentration and dosages of $KMnO_4$ for topical use and douching in domestic and farm animals.

In conclusion, the use of $KMnO_4$ in veterinary medicine should be based on careful consideration of its potential adverse effects on animals, and alternative disinfectants should be used when possible. Practitioners should carefully counsel users of potassium permanganate on how to use it safely. Only physiological and histological data are available about the use and misuse of $KMnO_4$, and there is need to study the molecular mechanism to determine its apparent benefits. In the future, researchers could determine the toxic effects of $KMnO_4$ in conjunction with traditional Chinese medication, miRNA, lncRNA, and circRNA therapy to understand how these therapeutic agents mediate effects in veterinary medicine.

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REFERENCES

- Abdulla AK, Al-Delemi D and Hassooni F, 2020. Treatment of uterine prolapse in cows by new method (uterine rubber ball). *Plant Arch* 20:1311-14.
- Abinaya P and Thangarasu S, 2017. Testing the efficacy of potassium permanganate as antiseptic for the control of bovine mastitis. *Int J Curr Microbiol Appl Sci* 6:609-11.
- Adhikari S, Sarkar B, Chatterjee A, et al., 2004. Effects of cypermethrin and carbofuran on certain hematological parameters and prediction of their recovery in a freshwater teleost, *Labeo rohita* (Hamilton). *Ecotoxicol Environ Saf* 58:220-26.
- Agrawal VK, Bansal A, Kumar R, et al., 2014. Potassium permanganate toxicity: A rare case with difficult airway management and hepatic damage. *Indian J Crit Care Med* 18:819.
- Al-Katib SR, Al-Azam AHA and Habeab SA, 2012. The effect of vitamin C on ovary of female white rats treated with $KMnO_4$. *Histological and physiological study*. *Kufa J Vet Med Sci* 3(2): 1-16.
- Allison R, 1957. Some new results in the treatment of ponds to control some external parasites of fish. *N Am J Aquac* 19:58-63.
- Anderson I, 2003. Should potassium permanganate be used in wound care? *Nurs Times* 99:61.
- Apaydin N, Kemiksiz E and Akcay A, 2019. Comparison of Manuka honey (Manuka Nd, G) and etacridine lactate (Rivanol) applications in the treatment of infected wounds in cats. *Acta Sci Vet* 47: 2019; Doi: [10.22456/1679-9216.90287](https://doi.org/10.22456/1679-9216.90287).
- Becker NA, O'Neill HA, Zimmerman JM, et al., 2000. *In vitro* and *in vivo* ligation-mediated polymerase chain reaction analysis of a polypurine/polypyrimidine sequence upstream of the mouse metallothionein-I gene. *J Biol Chem* 22:40218-25.
- Bigliardi PL, Alsagoff SA and El-Kafrawi HY, 2017. Povidone iodine in wound healing: A review of current concepts and practices. *Int J Surg* 44:260-68.
- Brandt MJ, Johnson KM, Elphinston AI, et al., 2016. Twort's Water Supply. Butterworth-Heinemann, Oxfordshire, UK.
- Brudenell JM, 1961. Potassium permanganate induced vaginal bleeding. *Br J Obstet Gynaecol* 68:115-18.
- Cabaniss CM and Clark JF, 1961. Potassium permanganate as an abortifacient: A 5-year review. *Am J Obstet Gynecol* 83:13-17.
- Chen JJ and Yeh HH, 2005. The mechanisms of potassium permanganate on algae removal. *Water Res* 39:4420-28.
- Cheng L and Chai Y, 2010. Analysis of vacuum sealing drainage complications during treatment of extremity wounds. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi (Chin J Reparative Reconstr Surg)* 24:1354-56.
- Chin G, Nicholson H, Demirel S, et al., 2022. Topical potassium permanganate solution use in dermatology: Comparison of guidelines and clinical practice. *Clin Exp Dermatol* 47:966-67.
- Chuanchuen R, Beinlich K, Hoang TT, et al., 2001. Cross-resistance between triclosan and antibiotics in *Pseudomonas aeruginosa* is mediated by multidrug efflux pumps: Exposure of a susceptible mutant strain to triclosan selects NF- κ B mutants overexpressing MexCD-OprJ. *Antimicrob Agents Chemother* 45:428-32.
- Conti P, Panara MR, Fridas S, et al., 1993. Inhibition of granuloma formation induced by potassium permanganate in the mouse by a specific human recombinant receptor antagonist for interleukin-1 (hrIL-1ra). *Cell Immunol* 147(2):446-57.
- Crandell RA, 1981. Bovine Papular Stomatitis. In: Ristic, M, McIntyre, WIM (Eds), *Diseases of Cattle in the Tropics: Economic and Zoonotic Relevance*. Springer Netherlands, Dordrecht 67-78; doi: 10.1007/978-94-011-9034-3 6.
- Darwish AM, Mitchell AJ and Straus DL, 2009. Evaluation of the therapeutic effect of potassium permanganate at early stages of an experimental acute infection of *Flavobacterium columnare* in channel catfish, *Ictalurus punctatus* (Rafinesque). *Aquac Res* 41:1479-85.
- Dash S, Bhojani I and Sharma S, 2018. A rare case of anal and perianal chemical burn in a child due to potassium permanganate crystals. *Drug Saf Case Rep* 5:10; doi: 10.1007/s40800-018-0072-5.
- Delgado-Enciso I, Madrigal-Perez VM, Lara-Esqueda A, et al., 2018. Topical 5% potassium permanganate solution accelerates the healing process in chronic diabetic foot ulcers. *Biomed Rep* 8:156-59.
- De-Mêo M, Laget M, Castegnaro M, et al., 1991. Genotoxic activity of potassium permanganate in acidic solutions. *Mutat Res Genet Toxicol Environ Mutagen* 260:295-306.
- Dörfel D, Maiwald M, Daeschlein G, et al., 2021. Comparison of the antimicrobial efficacy of povidone-iodine-alcohol versus chlorhexidine-alcohol for surgical skin preparation on the aerobic and anaerobic skin flora of the shoulder region. *Antimicrob Resist Infect Control* 10:1-9.
- Dumville JC, McFarlane E, Edwards P, et al., 2013. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. *Cochrane Database Syst Rev* 28(3): CD003949; doi: 10.1002/14651858.CD003949.pub3.
- Ebadian M, Al Haddabi A, Shpadaruk V, et al., 2022. National survey on the management of potassium permanganate by dermatologists. *Clin Exp Dermatol* 47:155-56.
- Echols K, Graves M, LeBlanc KG, et al., 2015. Role of antiseptics in the prevention of surgical site infections. *Dermatol Surg* 41:667-76.
- Enders AC, Enders RK and Schlafke S, 1963. An electron microscope study of the gland cells of the mink endometrium. *J Cell Biol* 18:405-18.
- Fan J, Daly R, Hobson P, et al., 2013. Impact of potassium permanganate on cyanobacterial cell integrity and toxin release and degradation. *Chemosphere* 92:529-34.
- Farhan AS and Mohammed MT, 2020. Histopathological changes in kidney and liver with oxidative stress and protection by plant extracts. *Veterinarija ir Zootechnika* 78:50-6.
- França IG, Ranzani-Paiva MI, Lombardi IV, et al., 2013. Toxic effect of potassium permanganate on *Oreochromis niloticus* based on hematological parameters and biomarkers of oxidative stress. *Int J Fish Aquac* 5:1-6.
- Fridas S, Trakatellis A, Karagouni E, et al., 1994. 4-Deoxyypyridoxine inhibits chronic granuloma formation induced by potassium permanganate *in vivo*. *Mol Cell Biochem* 136:59-63.

- Gallo P, Calderón TR and Lugo A, 1950. Vesicular stomatitis in Venezuela. *Rev de Med Vet Parsitol* 9:5-28.
- Glauber JR, 1656. Discovery of Potassium Permanganate 1959. *Prosperitas Germaniae* 93-94. Digitized December 6, 2021.
- Goldenheim PD, 1993. An appraisal of povidone-iodine and wound healing. *Postgrad Med J* 69:97-105.
- Gomes AC, 2012. "Too good to be true" the controversy over the use of permanganate of potash as an antidote to snake poison and the circulation of Brazilian physiology in the nineteenth century. *Bull Hist Med* 86:153-77.
- Gupta S, Sharma A and Singh M, 2018. Post-partum uterine eversion and its management in a doe: A case report. *Vet J* 90:67-68.
- Hasan T, Azizunnesa PM, Paul P, et al., 2017. Correction and management of vaginal prolapse in a cow by Buhner's technique. *Res J Vet Pract* 5 :1-4.
- Hibbard JS, 2005. Analyses comparing the antimicrobial activity and safety of current antiseptic agents: a review. *J Infus Nurs* 28:194-207.
- Hinderling PH, 2016. The pharmacokinetics of potassium in humans is unusual. *J Clin Pharmacol* 56:1212-20.
- Hunter AG, Henderson Jr BW and Dardiri AH, 1958. Granular vulvovaginitis: a review. *J Dairy Sci* 41:1024-32.
- Hu N, Wu XH, Liu R, et al., 2015. Novel application of vacuum sealing drainage with continuous irrigation of potassium permanganate for managing infective wounds of gas gangrene. *J Huazhong Univ Sci Technol Med Sci* 35:563-68.
- Jetter WW and Hunter FT, 1949. Death from attempted abortion with a potassium permanganate douche. *N Engl J Med* 240:794-98.
- Karthik R, Veerendranath HP, Wali S et al., 2014. Suicidal ingestion of potassium permanganate crystals: a rare encounter. *Toxicol Int* 21:331.
- Kass M, Viltrop A, Prakofiewa I, et al., 2022. Control of foot-and-mouth disease in a closed society: A case study of Soviet Estonia. *Front Vet Sci* 9:828-583.
- Khair A, Asaduzzaman M, Sultana Z, et al., 2018. Economic benefit in repeat breeder cows using intrauterine infusion of penicillin and estrus synchronization followed by timed artificial insemination. *J Adv Vet Anim Res* 5:454.
- Klimaszewska E, Wiczorek D, Lewicki S, et al., 2022. Effect of new surfactants on biological properties of liquid soaps. *Molecules* 27(17):5425; doi: 10.3390/molecules27175425.
- König B, Reimer K, Fleischer W, et al., 1997. Effects of Betaisodona (R) on parameters of host defense. *J Dermatol* 195:42-48.
- Korkut E, Saritas A, Aydin Y, et al., 2013. Suicidal ingestion of potassium permanganate. *World J Emerg Med* 4:73.
- Kumar M, 2014. Therapeutic management of bovine puerperal metritis in a cow. *Intas Polivet* 15:554-56.
- Kumar P, Dayal S, Tiwari R, et al., 2015. Vaginal prolapse in peri-partum primiparous murrah buffalo complicated into endometritis and cystitis: a case report. *Buffalo Bull* 34:153-59.
- Lachapelle JM, Castel O, Casado AF, et al., 2013. Antiseptics in the era of bacterial resistance: a focus on povidone iodine. *Clin Pract* 10:579.
- Lammert AC and Scott RB, 1954. Hazards in the intravaginal use of potassium permanganate. *Am J Obstet Gynecol* 68:854-59.
- Leeper DJ, Schultz G, Carville K, et al., 2012. Extending the TIME concept: what have we learned in the past 10 years? *Int Wound J* 9:1-9.
- Lipsky BA and Hoey C, 2009. Topical antimicrobial therapy for treating chronic wounds. *Clin Infect Dis* 49:1541-49.
- Mackeen AD, Packard RE, Ota E, et al., 2015. Antibiotic regimens for postpartum endometritis. *Cochrane Database Syst Rev* 2015(2): CD001067; doi: 10.1002/14651858.CD001067.pub3.
- Majtan I, 2011. Methylglyoxal—a potential risk factor of manuka honey in healing of diabetic ulcers. *Evid Based Compl Altern Med* 2011: 295494.
- Marsh SJ and Webster A, 1954. Vaginal hemorrhage from potassium permanganate burns. *Obstet Gynecol* 3:169-71.
- Martin EA and McFerran TA, 2014. Potassium permanganate. Oxford University Press, Oxford, UK.
- Ousey K and McIntosh C, 2009. Topical antimicrobial agents for the treatment of chronic wounds. *Br J Community Nurs* 14(Suppl 4): S6, S8, S10 passim. doi: 10.12968/bjcn.2009.14.Sup4.43909.
- Özyiğit F, Yıldız E, Çetiner M, et al., 2020. A rare case of poisoning: potassium permanganate toxicity. *Turk J Anaesthesiol Reanim* 48(3):248-50.
- Palaniappan V and Karthikeyan K, 2022. Potassium permanganate: a 'desert island drug' in dermatology. *Clin Exp Dermatol* 47:1650-57.
- Pathak R, Gupta VK, Saxena AC, et al., 2012. Management of hoof disorders in dairy farms. *Intas Polivet* 13:195-97.
- Philipp E, 1953. Vaginal bleeding due to potassium permanganate. *Lancet* 262:1278-80.
- Rai V, 2020. What is the evidence for the use of potassium permanganate for wound care? *Biol Pharm Bull* 58:71-74.
- Rowland PH, Valentine BA, Stebbins KE, et al., 1991. Cutaneous plasmacytomas with amyloid in six dogs. *Vet Pathol* 28:125-30.
- Saganuwan SA, Ahur VM and Yohanna CA, 2008. Acute toxicity studies of potassium permanganate in Swiss albino mice. *Niger J Physiol Sci* 23:31-35.
- Sebben JE, 1988. Sterile technique and the prevention of wound infection in office surgery part I. *J Dermatol Surg Oncol* 14:1364-71.
- Shefer T, Strebel A, Wilson T, et al., 2002. The social construction of sexually transmitted infections (STIs) in South African communities. *Qual Health Res* 12:1373-90.
- Stahl JB, Morse D and Parks PJ, 2007. Resistance of antimicrobial skin preparations to saline rinse using a seeded bacteria model. *Am J Infect Control* 35:367-73.
- Street RA, Kabera GM and Connolly C, 2018. Ethnopharmacological use of potassium permanganate in South African traditional medicine. *S Afr Med J* 108:187-89.
- Subramanya SH, Pai V, Bairy I, et al., 2018. Potassium permanganate cleansing is an effective sanitary method for the reduction of bacterial bioload on raw *Coriandrum sativum*. *BMC Res Notes* 11:1-5.
- Sukumar D, Vanan TT, Thennarasu A, et al., 2019. The effect of teat protects spray and potassium permanganate teat dip in curing subclinical mastitis in crossbred cows of Villupuram district of Tamilnadu. *J Appl Nat Sci* 11:738-42.
- Swearingen MC, Mehta A, Mehta A, et al., 2016. A novel technique using potassium permanganate and reflectance confocal microscopy to image biofilm extracellular polymeric matrix reveals non-eDNA networks in *Pseudomonas aeruginosa* biofilms. *Pathog Dis* 74:104.
- Türker D, Ustun E, Gunal S, et al., 2022. Cyanopropyl functionalized benzimidazolium salts and their silver N-heterocyclic carbene complexes: Synthesis, antimicrobial activity, and theoretical analysis. *Arch Pharm* 355:e2200041.
- Urban MV, Rath T and Radtke C, 2019. Hydrogen peroxide (H₂O₂): a review of its use in surgery. *Wein Med Wochenschr* 169:222-225.
- U.S. National Library of Medicine, 2008. Agency for Toxic Substances and Disease Registry; PubChem Compound Summary for CID 516875, Potassium permanganate. <https://pubchem.ncbi.nlm.nih.gov/compound/Potassium-permanganate>.
- Wang Y, Chen T, Gan Z et al., 2021. Metabolomic analysis of untargeted bovine uterine secretions in dairy cows with endometritis using ultra-performance liquid chromatography/quadrupole time-of-flight mass spectrometry. *Res Vet Sci* 139:51-58.
- Wattanathorn J, Kirisattayakul W, Suriharn B, et al., 2018. Functional drink containing the extracts of purple corn cob and pandan leaves, the novel cognitive enhancer, increases spatial memory and hippocampal neuron density through the improvement of extracellular signal regulated protein kinase expression, cholinergic function, and oxidative status in ovariectomized rats. *Rejuvenation Res* 21:431-41.
- WHO, 2004. Potassium Permanganate in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. Geneva, Switzerland: www.who.int/water_sanitation_health/dwq/chemicals/potassiumpermanganate.pdf.
- WHO. 2018. World Health Organization model list of essential medicines: 21st list, World Health Organization, Rome, Italy.
- Yadav MM, Narawade VE and Fulpagare YG, 2017. *Staphylococcus aureus* as a cause of bovine endometritis and its multiple drug resistance in organized dairy farm, Maharashtra. *Int J Multidiscip Res* 4:3-23.
- Yano BL, Johnson KH and Hayden DW, 1981. Feline insular amyloid: histochemical distinction from secondary systemic amyloid. *Vet Pathol* 18:181-87.
- Ziętek I, Dziegiel B, Wójcik A, et al., 2020. Effect of bathing in a 0.1% aqueous solution of ethacridine lactate on selected physiological parameters of *Cornu aspersum* Müller edible snails. *J Vet Res* 64:313