

# Influence of physical properties of injectable drugs based on Florfenicol and on the adaptability of application in animal husbandry

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**Abstract.** The article deals with the influence of the physical properties of Florfenicol preparations on the performance of procedures for its intramuscular administration in the conditions of livestock enterprises. It is indicated that the dynamic viscosity of the preparations has the greatest influence on the processability of performing this operation. The established dependence of the dynamic viscosity on the temperature showed that in the range from 16 to 26°C, the dynamic viscosity varies from one and a half to two times, depending on the type of preparation. At the same time, the rate of drug intake into the syringe and its injection is within acceptable limits.

## 1 Introduction

Currently, the Russian market of veterinary drugs presents a large number of injectable forms of Florfenicol from various manufacturers, differing in the concentration of the active substance.

These drugs have proven themselves well in the treatment of diseases of pigs and cattle caused by microorganisms sensitive to Florfenicol. If we talk about pig farming, it can be noted that injectable forms of Florfenicol are actively used to control such economically significant diseases for this branch of animal husbandry as pleuropneumonia actinobacillus suum, enzootic pneumonia, infection caused by *Staphylococcus aureus* [1, 2].

In the treatment of cattle with infectious diseases of bacterial etiology, the drugs are used for respiratory diseases caused by *Pasteurella multocida*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Micrococcus* spp., as well as for secondary bacterial infections [3, 4].

In some cases, with the direct mass use of the above-mentioned dosage forms of Florfenicol in the conditions of livestock enterprises, the question of the manufacturability of their use arises. In particular, there is a question of the influence of the characteristics of the drug on the performance of procedures for its intramuscular administration [5, 6].

The aim of this work was to study the physical properties of Florfenicol injectable drugs that can affect the technological efficiency of the drug injection procedure.

## 2 Materials and methods

One of the important physical indicators that characterize the technological possibility of using drugs for injection is their dynamic viscosity. At the same time, it is known that the viscosity of the components of the basis of these preparations largely depends on the temperature [7, 8].

To maintain different temperatures of the preparations, a thermostatic water bath was used to determine their viscosity.

The dynamic viscosity of the preparations (Pa·s) can be determined according to Stokes' law [9, 10] according to the calculation scheme (Fig. 1). According to this scheme, a steel ball placed in a vessel with the liquid under study, in order to determine the dynamic viscosity, is affected by  $\bar{F}_A$  – a pushing force (Archimedes' force),  $\bar{F}_V$  – a viscous friction force;  $\bar{m}\bar{g}$  – gravity.

In the projection on the vertical axis, the balance equation looks like:

$$F_A + F_v - mg = ma \quad (1)$$

where  $a$  is the acceleration of the ball, m/s<sup>2</sup>;

$m$  is the mass of the steel ball, kg.

However, after passing the mark A, the speed of the ball can be considered a constant value; therefore, the right part of equation (1) will become zero. Equation (1) will take the form:

$$F_A + F_v - mg = 0. \quad (2)$$

The mass of the steel ball can be determined taking into account the density of steel  $\rho_b = 7830$  kg/m<sup>3</sup> according to the formula:

$$m = \rho_b V_b = \frac{4}{3} \pi r^3 \rho_b \quad (3)$$

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where  $r$  is the radius of the ball.

Thus, the gravity will be determined:

$$mg = \frac{4}{3}\pi r^3 \rho_b g \quad (4)$$

The buoyant force is defined as:

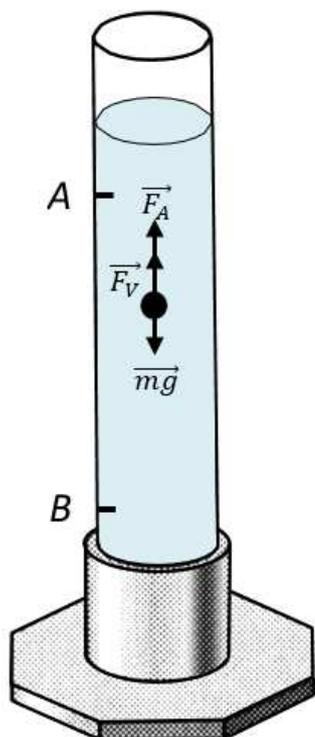
$$F_A = \frac{4}{3}\pi r^3 g \rho_l \quad (5)$$

where  $\rho_l$  is the density of the liquid, kg/m<sup>3</sup>.

The viscous friction force is determined by the formula:

$$F_v = 6\pi\mu r v \quad (6)$$

where  $v$  is the speed of the ball movement, m/s.



**Fig. 1.** Calculation scheme for determining the viscosity by the Stokes method:  $\vec{F}_A$  – Archimedes force,  $\vec{F}_V$  – viscous friction force,  $\vec{m}\vec{g}$  – gravity.

Substituting (4), (5) and (6) into equation (2), we obtain:

$$\frac{4}{3}\pi r^3 g \rho_l + 6\pi\mu r v - \frac{4}{3}\pi r^3 \rho_b g = 0 \quad (7)$$

From the upper label A to the lower one B, the distance between which  $l$  (Fig. 1) the ball movement is rectilinear uniform and the speed of movement  $v$  taking into account time  $t$ :

$$v = \frac{l}{t} \quad (8)$$

Expressing the radius of the ball  $r$  in terms of its diameter  $d$ :

$$r = \frac{d}{2} \quad (9)$$

Thus:

$$\mu = \frac{1}{18} d^2 g t \cdot \left( \frac{\rho_b - \rho_l}{l} \right) \quad (10)$$

where  $g$  – acceleration of gravity,  $g=9.8$  m/s<sup>2</sup>.

In this case, the diameter of the ball was determined using a microscope with an ocular micrometre. To determine the density of the liquid, a measuring cylinder was used.

To determine the rate of flow of the studied drugs when taking drugs into the syringe, a needle with a size of 1.5 x 30 mm and a 10 ml veterinary syringe of the "Record" type were used.

The effect of the viscosity of the above drugs on the rate of their removal from the syringe into the muscle was studied using injection needles with a size of 1.5x30 mm, 2.0x60 mm and a 10 ml veterinary type "Record" syringe.

### 3 Results and discussions

In practice, especially in the pig industry, there is an opinion that the injectable forms of Florfenicol from different manufacturers are injected at different rates, which can directly affect the procedure for intramuscular administration of the drug. For this purpose, we took the most commonly used drugs from various manufacturers - 30 % of Florox, Kadorex and Floron with a maximum concentration of Florfenicol for injectable forms of 300 mg / ml.

It is known that the dynamic viscosity of the preparations has the greatest influence on the rate of injection and injection. The value of this parameter of medicines was determined at different temperatures.

Despite the apparent similarity in the active substance and other components, the value of the dynamic viscosity of the preparations differs from each other (Table 1). According to Table 1, it can be seen that the least dynamic viscosity is possessed by the preparation Florox. The second and third places were occupied, respectively, by the preparations Kadorex and Floron 30 %.

In Florox, this dependence with a temperature change from 16 to 26°C was from 103.51 to 63.46, in Cadorex – 119.15 to 77.48, in Floron – from 129.75 to 92.52 mPa·s.

At the same time, the density of the preparations practically did not depend on the temperature. At the same time, the data of all preparations significantly exceeded the viscosity of water (Table 1), whose dynamic viscosity values are given here for comparison. According to Table 1, graphical dependences of the dynamic viscosity values on the temperature are plotted (Fig. 2).

In the temperature range from 16 to 26°C the obtained dependences are approximated by linear functions:

Floron:

$$\mu = -3.951T + 182.36 \quad (11)$$

with a confidence factor of approximation  $R = 0.931$ .

Kadorex:

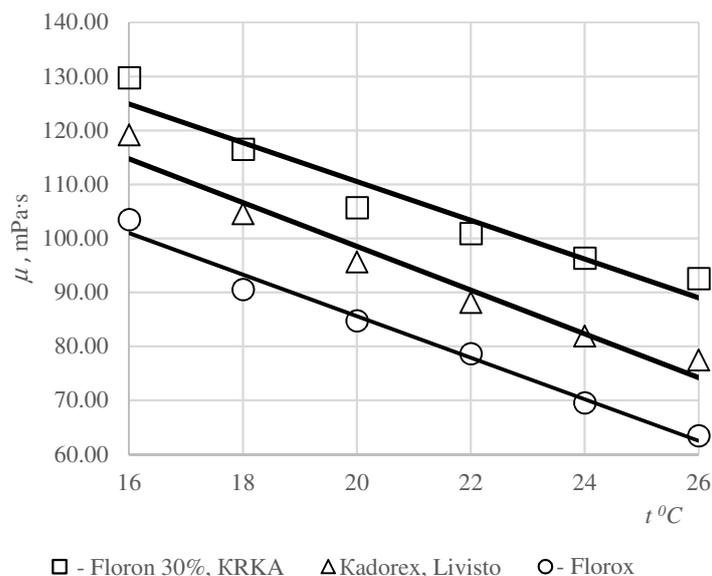
$$\mu = -4.053T + 179.59 \quad (12)$$

with a confidence factor of approximation  $R = 0.96$ .

Florox:

$$\mu = -3.849T + 162.56 \quad (13)$$

with a confidence factor of approximation  $R = 0.984$ .



**Fig. 2.** Dependence of the dynamic viscosity of veterinary drugs on temperature

**Table 1.** The value of the dynamic viscosity and density of veterinary drugs

Name of the drug	Water	Florox	Kadorex Livisto	Floron 30% KRKA
The density of the drug, g/cm <sup>3</sup>	1	1.154±0.012	1.138±0.011	1.156±0.013
Viscosity of the tested preparations at different ambient temperatures, mPa·s	16°C	103.51±4.26	119.15±6.31	129.75±7.17
	18°C	90.53±3.75	104.54±5.04	116.48±6.88
	20°C	84.75±2.81	95.64±4.89	105.70±5.03
	22°C	78.65±1.92	88.13±4.53	100.87±5.33
	24°C	69.51±1.86	83.92±4.05	96.35±4.97
	26°C	63.46±1.44	77.48±3.95	92.52±4.53

**Table 2.** Results of determining the rate of injection of Florfenicol-based injectable drugs into the syringe (the drugs were taken through a needle of 1.5 x 30 mm)

Name of the drug	Data on the time in seconds of injection of 4.0 ml of Florfenicol-based injectable drugs at ambient temperature:	
	20°C	24°C
Florox	12.39±1.23	7.52± 0.89
Kadorex Livisto	16.06± 1.56	10.07± 1.01
Floron 30% KRKA	23.05± 2.01	17.05± 1.69

The next step was determining the effect of the viscosity of the drugs on the speed of a passage through an injection needle with a diameter of 1.5 mm at a temperature of 20°C and 24°C in a volume of 4.0 ml (the average therapeutic dose of the drug per animal). The results of the studies presented in Table 2 indicate that the drugs similar in active substance and excipients, Florox and Floron 30%, had approximately the same time of taking the drugs into the syringe at a temperature of 20°C, but it decreased almost 2 times at a temperature of 24°C.

At the same time, the rate of intake of Kadorex into the syringe at a temperature of 20°C and 24°C was 16.06 and 10.07 seconds, respectively. The data on the difference in the time of sampling of drugs may be due to the auxiliary substances that are part of the drugs and their concentration. Propylenglycol, Dimethylsulfoxidum, Polyethyleneglycol are those for the preparations Florox and Floron of 30 %, and for the preparation Kadorex - Methyl-N-II-Pyrrolidone( NMP), Alcoholum Benzylicum, formalis Glycerinum.

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**Table 3.** Time of administration of Florfenicol-based injectable drugs

Name of the drug	The time of injection with a 4.0 ml syringe of injectable drugs at an ambient temperature of 20.0 °C and the size of the needle:	
	1.5x30 mm	2.0x60 mm
Florox	7.54 ±0.52	6.53 ±0.51
Kadorex Livisto	8.54 ±0.63	7.56 ±0.56
Floron 30% KRKA	9.60 ±0.64	8.06 ±0.81

If we compare the speed of drug intake through the needle, it is obvious that the viscosity can affect the time of drug intake into the syringe, but it is not so critical in the technology of mass treatment of animals. This statement is also true in the case of intramuscular injection of drugs from a syringe. According to table 3, the time spent on one injection of the analyzed drugs at an ambient temperature of 20 °C was slightly different and was about 6.53 – 8.06s for a needle size of 1.5x30 mm, 7.54-9.60s for a needle size of 2.0x30 mm.

With intramuscular administration of the drugs through a 2.0 x 60 mm needle, the shortest administration time was for the drug Kadorex (7.52 s), while for Floron 30% and Florox it was 8.06 and 8.54 seconds, respectively.

## 4 Conclusion

The conducted studies have shown that the value of the dynamic viscosity of the studied preparations in the temperature range from 16 to 260C is within: for Florox – 103.51 - 63.46, for Kadorex – 119.15 - 77.48, for Floron – 129.75 - 92.52 mPa·s.

According to the results of the studies, it was found that the rate of recruitment (the volume of the drug injected into the syringe per unit of time) of the analyzed injection drugs based on Florfenicol depends on the dynamic viscosity. With an increase in the value of the dynamic viscosity of these drugs, the speed of their recruitment into the syringe decreases. The same analogy can be traced with intramuscular injection of drugs. As a result, the economic efficiency of mass treatment of animals with the analyzed drugs may decrease.

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