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THE INFLUENCE OF ALPHA-ADRENERGIC RECEPTORS ON UTERUS MYOELECTRICAL ACTIVITY IN SHEEP NON - SENSITISED AND SENSITISED WITH STILBOESTROL

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ABSTRACT

The research was conducted on 7 inter-breed hybrid sheep, at the age from 10 to 48 months and of the body mass of 32-47 kg, which had bipolar electrodes implanted to the uterus shank and horns. The registration of uterus myoelectrical activity was performed on non-sensitised sheep and 24-48 hours after stilboestrol sensitisation, with the use of electroencephalograph. After recording the output activity, the sheep were administered in continuous infusion: adrenaline – agonist of alpha and beta – adrenergic receptors in the dose of 0.12-0.18 $\mu g \cdot kg^{-1} \cdot min^{-1}$; detomidin – agonist of alpha-adrenergic receptors in the dose of 0.1 – 1.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$; phenylephryn – agonist of $alpha_1$-adrenergic receptors in the dose of 2.1 – 2.9 $\mu g \cdot kg^{-1} \cdot min^{-1}$; xylasine – agonist

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of alpha$_2$-adrenergic receptors in the dose of 0.5 – 4.0 μg · kg^{-1} · min^{-1}; prazosin – antagonist of alpha$_1$-adrenergic receptors in the dose of 20-50 μg kg^{-1}; yohimbine – antagonist of alpha$_2$-adrenergic receptors in the dose of 160-240 μg · kg^{-1}; phentolamine – antagonist of alpha$_1$- and alpha$_2$- adrenergic receptors in the dose of 0.8 – 0.9 μg · kg^{-1}. The experiment results are presented in the inclosed drawings. The conducted research demonstrated that both subtypes of alpha$_1$ and alpha$_2$ adrenergic receptors occur in uterus of sheep during anestrus, sensitised with stilboestrol. The activation of these receptors cause the increase of uterus myoelectrical activity.

Key words: sheep, uterus, myoelectrical activity, alpha – adrenergic receptors

INTRODUCTION

Detailed knowledge of molecular receptor influences on uterus activity of various animal breeds is necessary during applying medicines from the so-called group of agonists and antagonists of these receptors. Adrenolitics and adrenomimetics generate a specific influence through alpha or beta – adrenergic receptors. There are brand differences in the distribution and quantity of these receptors in various organs (17). As for farm animals, there is a lack of detailed data on adrenergic receptor concentration in uterus muscular coat in various functional conditions of this organ – during the ovarian cycle, during pregnancy, delivery and during puerperium. Learning the receptor behaviour of females in the periods mentioned above enables the uterus movement control of particular domestic animal brands (5). Numerous publications concerning adrenergic receptors in domestic animal uterus have not thoroughly explained their influence on myoelectrical activity change of uterus in various physiological and pathological conditions.

The aim of this research was to demonstrate the influences from alpha- adrenergic receptors on uterus myoelectrical activity of sheep during anestrus.

MATERIALS AND METHODS

Seven inter–breed hybrid ewes at the age from 10 to 48 months and of the body mass of 32-47 kg, underwent operations, during which bipolar platinic electrodes were subserously implanted to uterus horns and shank (10). The research began 2 weeks after the treatment. The registration of uterus myoelectrical activity was conducted by the use of Reega Duplex TR XVI electroencephalograph, with the time-constant of 0.01 s. The research was performed on sheep non-sensitised and sensitised with Stilboestrol-Polfa applying it intramuscularly in the dose of 0.04 mg · kg^{-1}. During the experiments, physiological fluid was intravenously applied in continuous infusion (through a catheter introduced to the outer cervix vein before the experiment), and one of the below mentioned medicines was administered after recording the output curve of uterus myoelectrical activity: adrenaline (Injec. Adrenalini 0.1% - Polfa) – agonist of alpha and beta-adrenergic receptors in the dose of 0.12-0.18 μg · kg^{-1} · min^{-1}; detomidin (Detomidin.hydrochloric – Domosedan – Lããke Farmos company) – agonist of alpha$_2$-adrenergic receptors in the dose of 0.1-1.1 μg · kg^{-1} · min^{-1}; phenylephryn (Phenylephryn iniection B.P - Boots Company PLC) – agonist of alpha$_1$-adrenergic receptors in the dose of 2.1 – 2.9 μg · kg^{-1} · min^{-1}; xylasine (Xylazine 2% - Scar Vet Company) – agonist of alpha$_2$-adrenergic receptors in the dose of 0.5 – 4.0 μg · kg^{-1} · min^{-1}; prazosin (Prazosin HCI, USP grade – RBI) – antagonist of alpha$_1$-adrenergic receptors in the dose of 20-50 μg kg^{-1}; yohimbine (Yohimbine HCI – RBI) – antagonist of alpha$_2$-adrenergic receptors in the dose of 160-240 μg · kg^{-1}; phentolamine (Regitine Ciba – phento-lamin.methanosulfonic.) – antagonist of alpha$_1$- and alpha$_2$- adrenergic receptors in the dose of 0.8 – 0.9 μg · kg^{-1}. The applied medicine doses were specified individually for each sheep.

In general, 65 experiments were conducted. The obtained electrouterograms were assessed by a visual method (4).

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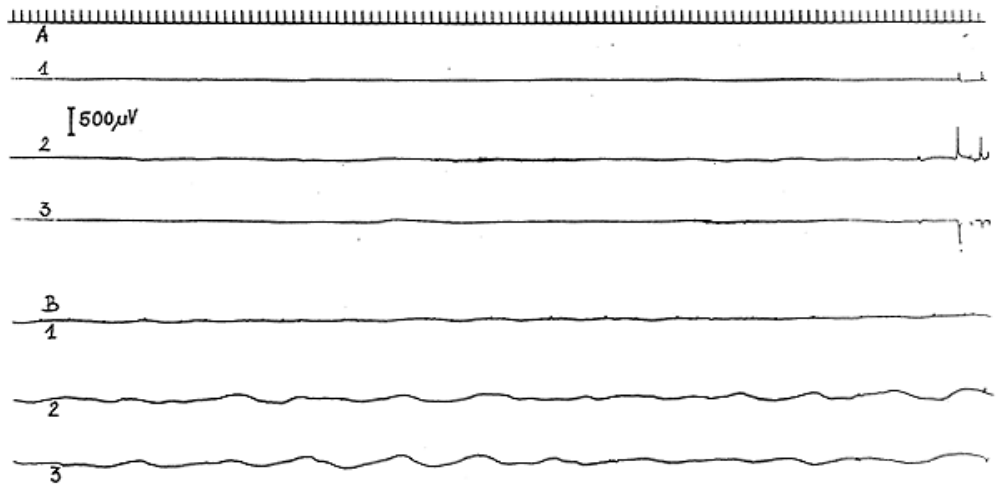
RESULTS AND DISCUSSION

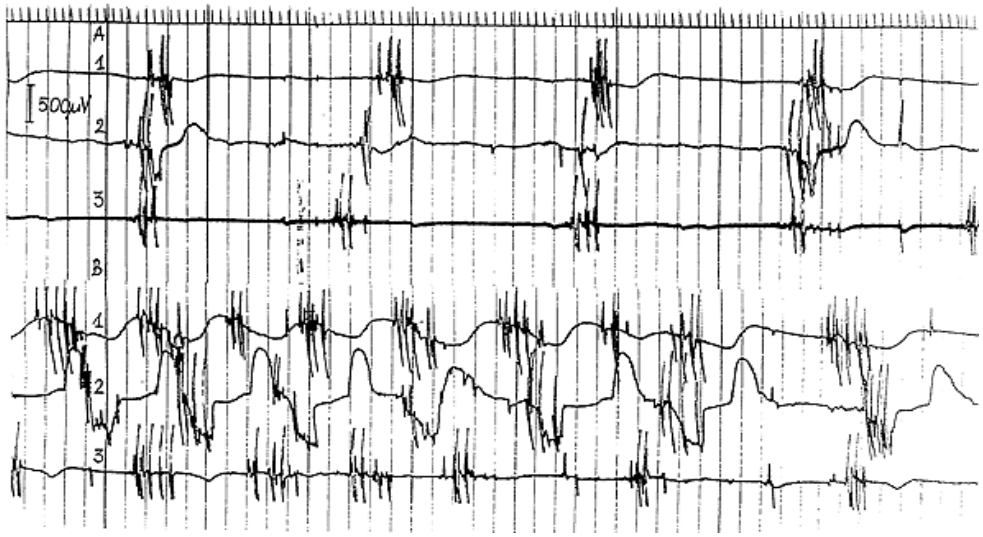
The performed experiments showed that there was a lack of action potentials in uterus of sheep during anestrus, non-sensitised with stilboestrol (Figure 1A). Similar results were gained by other authors (1, 2, 7, 8, 20, 21). During this time the applied agonist of $alpha_1$ or $alpha_2$-adrenergic receptors did not cause any changes in uterus myoelectrical activity record (Figure 1B). Prud-homme (12) suggests on the basis of his research that alpha-adrenergic receptors are hormone-dependent (on estrogens), which is confirmed by our observations.

Figure 1



Sheep sensitised with stilboestrol revealed cyclic activity both in uterus shank and horns (Figure 2A). The frequency of functional potential spindles in 24th hour after the sensitisation ranged from 5 to 8 min^{-1}. The intensity of this activity – amplitude and needle discharge frequency – was increased 24 hours after the sensitisation and decreased to a total atrophy in 7th – 8th 24-hour period. The results of our research are confirmed by data obtained by other authors (7, 9, 15, 19), who proved the stimulating influence of estrogens on uterus cramping of sheep. Lye et al. (6) are of the opinion that estrogens of these animals act diphasically – first they inhibit the uterus cramps, and then they stimulate them.

Figure 2



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The applied phenylephryn, a selective agonist of alpha$_1$-adrenergic receptors, revealed the presence (in sheep miometrium sensitised with stilboestrol) of receptors of this type. The agonist caused an intensified uterus myoelectrical activity in sensitised sheep (Figure 2). The reaction duration varied from 3 to 5 minutes depending on the dose. After blocking alpha$_1$-adrenergic receptors with a selective antagonist – prazosin (3,16) or with an antagonist of both alpha-adrenergic receptor subtypes (alpha$_1$ and alpha$_2$) – phentolamine, the applied phenylephryn did not cause any reaction in uterus myoelectrical activity (Figure 3). The achieved results confirm the alpha$_1$-adrenergic receptor presence in sheep sensitised with stilboestrol. Our observations concerning these receptors comply with Prud-home's research (12). Investigations on the alpha$_2$-adrenergic receptor presence in sheep miometrium were also conducted by the use of two selective antagonistic medicines – detomidin and xylasine. Detomidin applied to sensitised sheep intensified the uterus myoelectrical activity (Figure 4). In the electrouterographic record the frequency of the needle discharge increased while the intervals between discharge cycles shortened. The reaction duration oscillated between 3 and 5.5 minutes. After blocking alpha$_2$-adrenergic receptors with yohimbine – a selective agonist, the applied detomidin did not affect the electrouterographic record (Figure 5). After blocking both subtypes of alpha-adrenergic receptors (alpha$_1$ and alpha$_2$) with phentolamine, the applied detomidin did not cause any changes in uterus myoelectic activity, either. Xylasine applied to sensitised sheep caused, similarly as detomidin, the increase of uterus myoelectrical activity. In electrouterographic record the frequency of needle discharges also increased. The reaction duration ranged from 4 to 6 minutes depending on the dose. After blocking alpha$_2$-adrenergic receptors with yohimbine there was no characteristic reaction after applying xylasine. Also after blocking alpha$_1$ and alpha$_2$-adrenergic receptors with phentholamine there were no changes in the electrouterographic record after applying the agonist mentioned above. The obtained results indicate that both subtypes of alpha-adrenergic receptors (alpha$_1$ and alpha$_2$) occur in sheep sensitised with stilboestrol, which is confirmed by data gained by other authors (11, 12, 13).

Figure 3

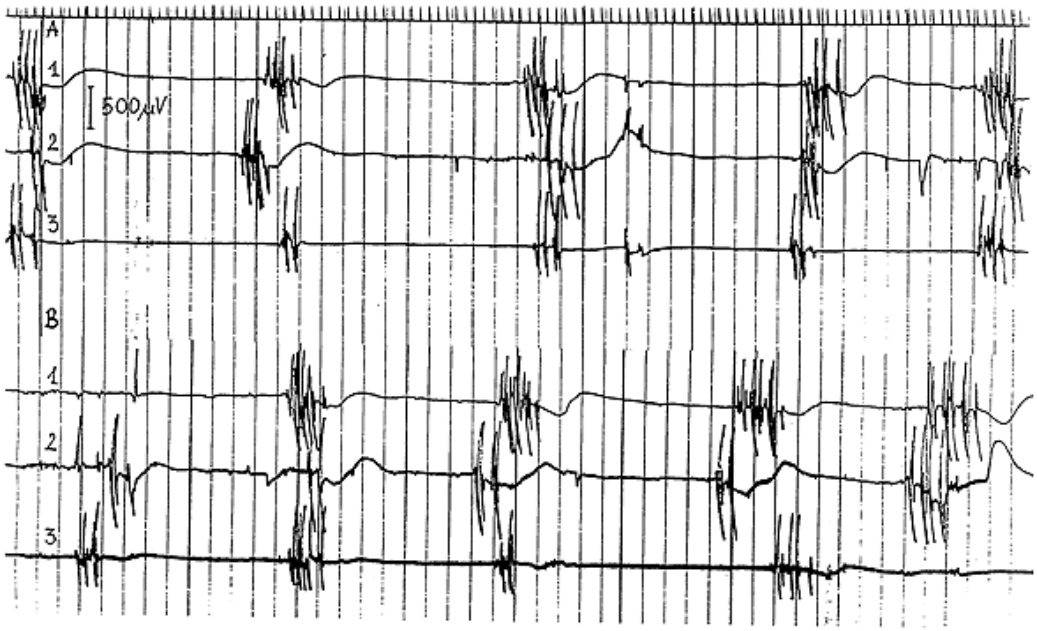

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Figure 4

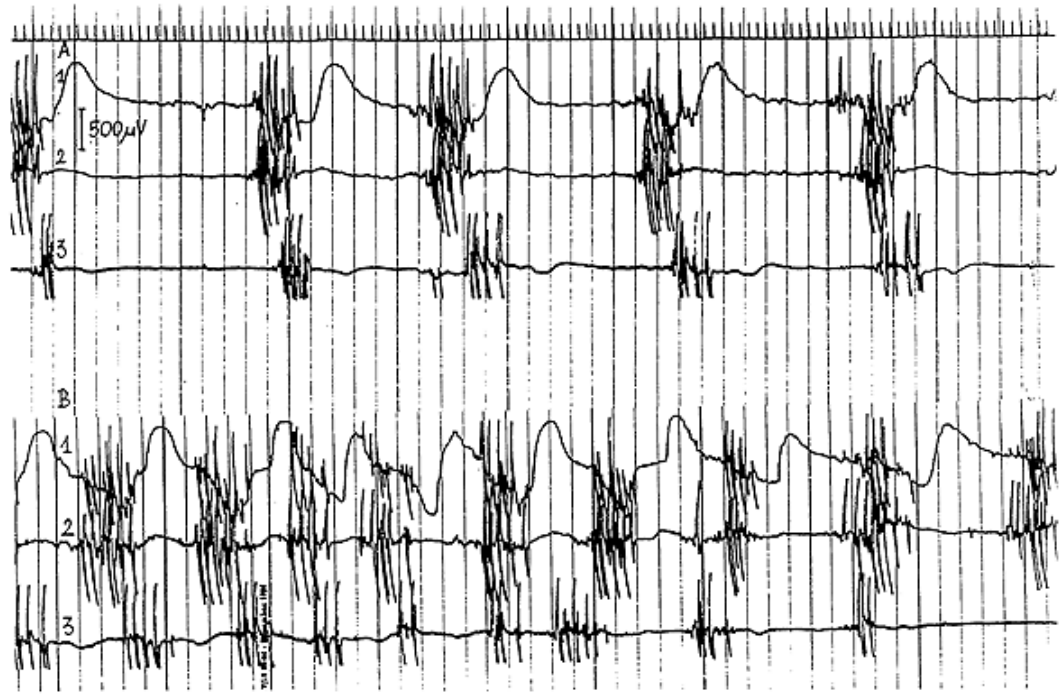
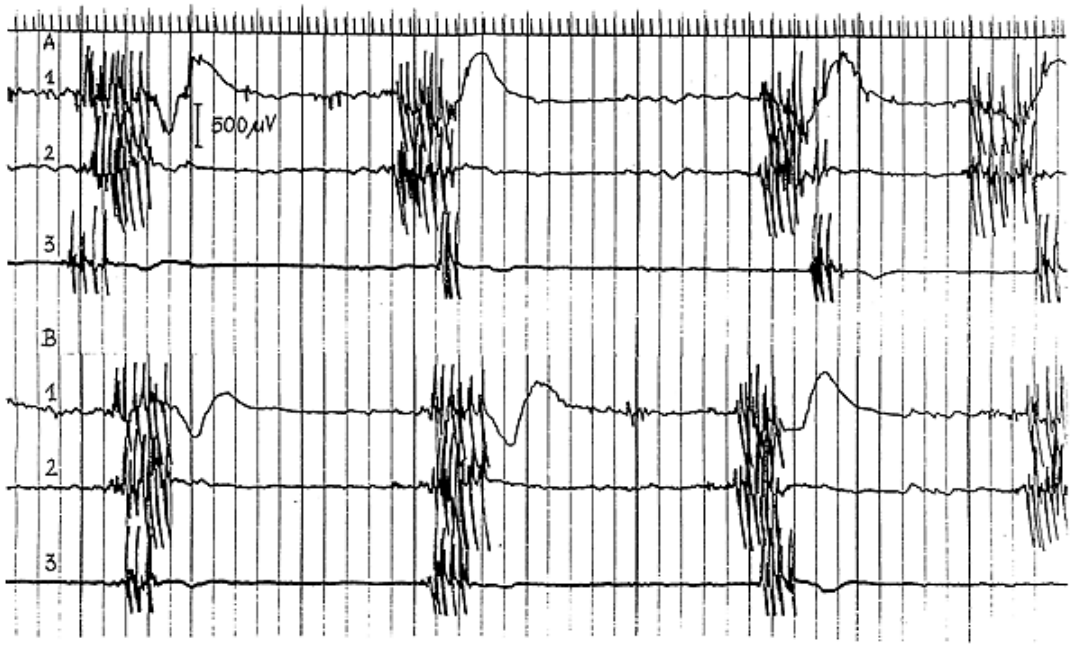


Figure 5



After sensitising ewes with stilboestrol the applied adrenaline intensified the uterus myoelectrical activity (Figure 6). The reaction time depended on the dose of the applied hormone. Its duration amounted to 2 to 6 minutes. The adrenaline applied after blocking alpha$_1$-adrenergic receptors with prazosin caused, to a lower extent, the stimulation of uterus myoelectrical activity (Figure 7). However, after blocking both subtypes of alpha-adrenergic receptors (alpha$_1$ and alpha$_2$) with phentolamine, the reapplied adrenaline did not cause any changes in uterus myoelectrical activity. The conducted research proves that in miometrium of sheep during anestrus, sensitised with stilboestrol, there are both subtypes of alpha-adrenergic receptors. The obtained lower extent of uterus myoelectrical activity stimulation

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after applying adrenaline and after blocking alpha$_1$-adrenergic receptors demonstrate that these receptors (alpha1-adrenergic) occur in miometrium of sheep in a considerably larger quantity than alpha$_2$-adrenergic receptors. Our observations stay in accordance with Rang and Dale's data (14) and also the data of Sergeew and Simanowski (18).

Figure 6

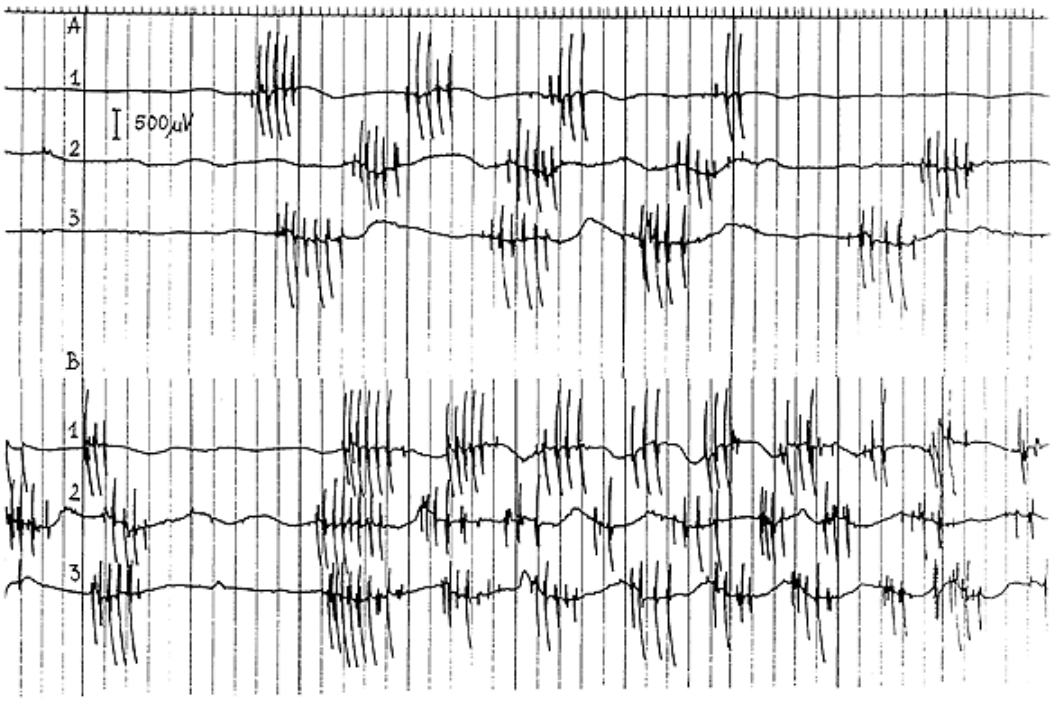
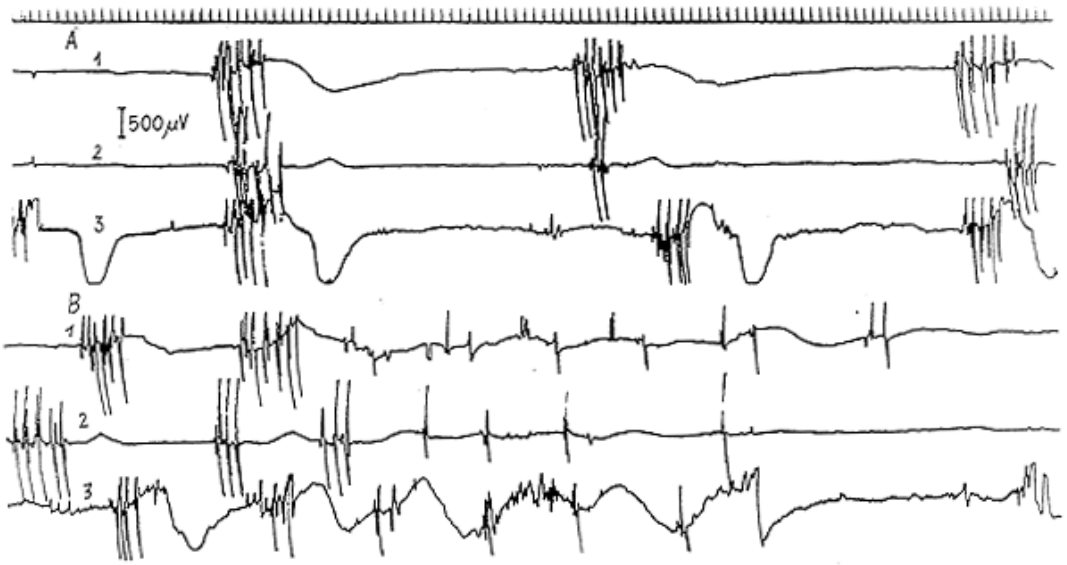


Figure 7



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CONCLUSIONS

1. Both subtypes of alpha$_1$ and alpha$_2$-adrenergic receptors occur in the uterus of sheep during anestrus sensitised with stilboestrol.
2. The stimulation of alpha1 or alpha2-adrenergic receptors cause the uterus myoelectrical activity increase.

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