Effects of imidazoline and nonimidazoline alpha-adrenergic agents, including xylazine, medetomidine, yohimbine, tolazoline, and atipamezole, on aggregation of bovine and equine platelets

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Objective—To investigate effects of various imidazoline and nonimidazoline α-adrenergic agents on aggregation and antiaggregation of bovine and equine platelets.

Sample—Blood samples obtained from 8 healthy adult cattle and 16 healthy adult Thoroughbreds.

Procedures—Aggregation and antiaggregation effects of various imidazoline and nonimidazoline α-adrenergic agents on bovine and equine platelets were determined via a turbidimetric method. Collagen and ADP were used to initiate aggregation.

Results—Adrenaline, noradrenaline, or α-adrenoceptor agents alone did not induce changes in aggregation of bovine or equine platelets or potentiate ADP- or collagen-induced platelet aggregation. Adrenaline and the α2-adrenoceptor agonist clonidine had an inhibitory effect on ADP- and collagen-induced aggregation of bovine platelets. The α1-adrenoceptor antagonists phentolamine and yohimbine also inhibited collagen-induced aggregation of bovine platelets. Noradrenaline, other α-adrenoceptor agonists (xylazine, oxymetazoline, and medetomidine), and α-adrenoceptor antagonists (atipamezole, idazoxan, tolazoline, and prazosin) were less effective or completely ineffective in inhibiting ADP- and collagen-induced aggregation of bovine platelets. The imidazoline α1-adrenoceptor agonist oxymetazoline submaximally inhibited collagen-induced aggregation of equine platelets, and the α2-adrenoceptor antagonist idazoxan, along with phentolamine and yohimbine, also inhibited collagen-induced aggregation of equine platelets. The imidazoline compound antazoline inhibited both ADP- and collagen-induced aggregation of equine platelets.

Conclusions and Clinical Relevance—Several drugs had effects on aggregation of platelets of cattle and horses, and effective doses of ADP and collagen also differed between species. The α2-adrenoceptor agonists (xylazine and medetomidine) and antagonists (tolazoline and atipamezole) may be used by bovine and equine practitioners without concern for adverse effects on platelet function and hemostasis. (Am J Vet Res 2013;74:395–402)
ole α₁-adrenoceptor agonist, has a complex effect on platelets. For example, clonidine binds with high affinity to α₁-adrenoceptors on platelets but induces only limited platelet aggregation, which is in contrast to the effect of endogenous agonists such as adrenaline. In addition, clonidine potentiates ADP-induced aggregation of human platelets but has inhibitory activity against adrenaline- and noradrenaline-induced platelet aggregation. Although the mechanism underlying these conflicting actions of clonidine is unclear, it has been suggested that imidazole compounds may interact with non-α₁-adrenoceptor binding sites on platelets. Two clonidine-related drugs have been reported to inhibit platelet adenylyl cyclase through non-α₁-adrenoceptor mechanisms because their effects were not blocked by yohimbine. Moreover, clonidine-displacing substance, which was extracted from bovine brain tissue, was recognized as a noncatecholamine endogenous ligand for α₁-adrenoceptors and interacts with nonadrenoceptor sites in the brainstem, as determined by use of tritiated para-aminoclonidine. Non-adrenergic, imidazoline-prefering binding sites (I₁ and I₂ receptors) that are pharmacologically distinct from α₁-adrenoceptors have been detected in human platelets. To the authors’ knowledge, few studies have been conducted to clarify the direct effects of imidazoline agents on platelet aggregation, although some studies have indicated that there may be a dysregulation of α₁-adrenoceptors and I₁ receptors on platelets of humans with depression.

In contrast to effects in humans, adrenaline alone in cattle does not induce platelet aggregation or potentiate platelet aggregation induced by other platelet agonists such as ADP, collagen, thrombin, or platelet activating factor. Because bovine platelets lack the open canalicular system found in platelets of humans and other species, it has been proposed that bovine platelets are useful in the examination of platelet secretion. Adrenaline does not function as a platelet agonist in cattle, but it does act as a platelet agonist in horses. Equine platelets have been used to investigate platelet signaling pathways. Therefore, bovine and equine platelets are suitable for use in the examination of platelet aggregation. In addition, α₁-adrenoceptor agonists are commonly used for sedation, analgesia, and premedication purposes in bovine and equine practice. However, there has been only limited investigation of the pharmacological action of α₁-adrenergic agents on platelet functions and identification of adrenoceptors on bovine and equine platelets. In addition, it is unclear whether imidazolines have any bioactivity effects on bovine and equine platelets.

Comparative studies on the effects of imidazolines on aggregation of bovine and equine platelets may be important for characterizing platelet receptors and may be useful for elucidating the biological function of imidazoline receptors. Furthermore, the imidazoline-derivative drugs that control platelet aggregation may have clinical benefits, such as for a hypercoagulation state accompanied by hypercatalcholamemia because catecholamines have a stimulatory effect on platelet aggregation. The purpose of the study reported here was to investigate aggregation and antiaggregation effects of various imidazoline or nonimidazoline α₁-adrenergic agents on bovine and equine platelets.

**Materials and Methods**

**Sample**—Blood samples for use in the study were collected from 8 healthy adult cattle (5 Japanese Black cattle and 3 Holsteins) and 16 healthy adult Thoroughbreds (12 geldings and 4 mares). For experiments on ADP- and collagen-induced platelet aggregation, jugular blood samples were collected into plastic syringes that contained 3.5% sodium citrate solution (1 part anticoagulant:9 parts blood). Blood samples were centrifuged at 100 to 120 × g for 15 minutes to obtain PRP. The PPP was obtained by centrifugation of PRP at 1,500 × g for 15 minutes. The final platelet count was adjusted to 25 to 30 × 10⁸ platelets/µL via dilution with autologous PPP. The study protocol was approved by the Animal Research Committee of Tottori University.

**Aggregation experiments**—Platelet aggregation experiments were performed as previously described. Briefly, a turbidimetric method was used. Percentage aggregation was determined after addition of aggregation agents and was standardized via the assumption that PPP and PRP represented 100% and 0% light transmission, respectively. An aliquot (200 µL) of PRP was placed in an aggregometer at 37°C, and then an aliquot (22 µL) of each aggregation agent (α-noradrenaline, antazoline HCl, clonidine HCl, idazoxan HCl, oxymetazoline HCl, prazosin HCl, tolazoline HCl, yohimbine HCl, phentolamine mesylate, atipamezole HCl, medetomidine HCl, xylazine HCl, ADP, and collagen) was added to the PRP 0.5 to 1 minute later. Adrenaline and noradrenaline were dissolved in 0.04 M HCl solution and then diluted with saline (0.9% NaCl) solution. Prazosin was dissolved in sterile distilled water and then diluted with sterile saline solution. All other drugs were dissolved in saline solution. In addition, saline solution was used throughout as a negative control agent.

To examine the stimulatory or inhibitory effects of α₁-adrenergic agents on ADP- and collagen-induced aggregation, α₁-adrenergic agents were added 1 minute before the addition of ADP or collagen. Maximum percentage aggregation during the 10-minute interval after the addition of ADP or collagen was recorded.

**Statistical analysis**—All data were expressed as the mean ± SE; each mean represented results for 5 animals. Statistical analysis was performed with commercially available software. A 1-way ANOVA followed by the Dunnett post hoc test was used for intragroup comparisons of concentration-related aggregation. For the inhibitory effect of agents on platelet aggregation, IC₅₀ was determined from the concentration-response curve. An ANOVA was used to compare IC₅₀ values. Depending on the F value, the Student t test of Wilcoxon–Mann–Whitney test was used to determine significance. Differences were considered significant at values of P < 0.05.

**Results**

Aggregation effects of α₁-adrenergic agents on bovine platelets—Adrenaline, noradrenaline, oxymetazo-
line, clonidine, medetomidine, xylazine, yohimbine, phen tolamine, atipamezole, idazoxan, tolazoline, and prazosin at concentrations from 0.1 nmol/L to 100 µmol/L did not stimulate aggregation of bovine platelets (data not shown).

Aggregation effects of ADP or collagen on bovine and equine platelets—Both ADP and collagen induced aggregation of bovine and equine platelets in a dose-dependent manner. In bovine platelets, the aggregation effect of ADP at concentrations exceeding 1 µmol/L or collagen at concentrations exceeding 5 µg/mL was significantly different from values for the control (saline solution) agent (Figure 1). On the basis of these results, examination of the stimulatory effects of α-adrenergic agents on ADP- or collagen-induced platelet aggregation would necessitate a concentration of ADP (2 µmol/L) or collagen (3 µg/mL) that caused almost submaximal aggregation (<25%) to induce platelet aggregation because these concentrations of ADP and collagen induced optimal aggregation responses in most platelet preparations. In contrast, a concentration of ADP (20 µmol/L) or collagen (10 µg/mL) that induced almost complete platelet aggregation (>80% aggregation) was chosen to examine the inhibitory effects of α-adrenergic agents on ADP- or collagen-induced platelet aggregation.

Similarly, the aggregation effect in equine platelets at concentrations of ADP exceeding 0.5 µmol/L or collagen exceeding 1.5 µg/mL was significantly different from values for the control agent (Figure 1). A concentration of ADP (0.5 µmol/L) or collagen (1.5 µg/mL) that induced almost submaximal aggregation (approx IC25) was chosen to induce platelet aggregation because these concentrations of ADP and collagen induced optimal aggregation responses in most equine platelet preparations.

Effects of imidazoline and nonimidazoline α-adrenoceptor agents on aggregation of bovine platelets induced by a high dose of ADP or collagen—Concentration–effect curves of imidazoline α-adrenoceptor agonists on aggregation of bovine platelets induced by a low dose of ADP (2 µmol/L) and collagen were plotted (Figure 2). An imidazoline α-adrenoceptor agonist (oxymetazoline) potentiated platelet aggregation induced by low-dose ADP in a dose-dependent manner, whereas the imidazoline α-adrenoceptor agonist clonidine, at a concentration of 100 µmol/L, completely inhibited low-dose ADP–induced platelet aggregation. Other α-adrenoceptor agonists, including adrenaline and noradrenaline, were ineffective against the low-dose ADP–induced aggregation of bovine platelets. In addition, a wide range of concentrations (0.1 nmol/L to 100 µmol/L) of the α-adrenoceptor antagonists yohimbine, phentolamine, atipamezole, idazoxan, tolazoline, and prazosin were also ineffective against the low-dose ADP–induced aggregation of bovine platelets.

In contrast to results for the low-dose ADP–induced platelet aggregation, all of the α-adrenoceptor agents were ineffective against low-dose collagen–induced aggregation of bovine platelets.

Effects of imidazoline and nonimidazoline α-adrenoceptor agents on aggregation of bovine platelets induced by a high dose of ADP or collagen—Concentration–effect curves of imidazoline and nonimidazoline α-adrenoceptor agents on aggregation of bovine platelets induced by a high dose of ADP (20 µmol/L) or collagen (10 µg/mL) in citrated plasma were plotted (Figure 3). The α-adrenoceptor agonist clonidine significantly inhibited high-dose ADP–induced platelet aggregation and permitted determination of IC50 values. Adrenaline also caused a small inhibition (approx IC50) of high-dose ADP–induced aggregation of bovine platelets, whereas noradrenaline did not have any effect on aggregation of bovine platelets. The remaining α-adrenoceptor agonists (xylazine, oxymetazoline, and medetomidine) and all of the α-adrenoceptor antagonists evaluated were ineffective against high-dose ADP–induced aggregation of bovine platelets.

In contrast with results for the high-dose ADP–induced platelet aggregation, inhibitory activity by α-adrenoceptor agents was clearly evident on high-dose collagen–induced aggregation of bovine platelets. Adrenaline and the imidazoline α-adrenoceptor agonist clonidine (1 to 100 µmol/L) significantly inhibited (by >50%) high-dose collagen–induced aggregation of bovine platelets (Figure 3; Table 1). The imidazoline α2-adrenoceptor antagonist phentolamine and the nonimidazoline α2-adrenoceptor antagonist yohimbine (10 to 100 µmol/L) also had an inhibitory effect of >50% on the high-dose collagen–induced platelet aggregation. The remaining α-adrenoceptor agents did not have a clear effect on collagen–induced aggregation of bovine platelets.
The IC_{25} and IC_{50} values obtained for the inhibition of high-dose collagen–induced aggregation of bovine platelets were summarized (Table 1). The IC_{25} and IC_{50} values were not attained for noradrenaline, xylazine, oxymetazoline, medetomidine, atipamezole, idazoxan, tolazoline, or prazosin. The inhibitory potencies (based on the IC_{50} values) of phentolamine were 4- to 11-fold as high as those of adrenaline, clonidine, and yohimbine.

Effects of imidazoline and nonimidazoline \(\alpha\)-adrenoceptor agents on ADP- or collagen-induced aggregation of equine platelets—Concentration–effect curves of imidazoline and nonimidazoline \(\alpha\)-adrenoceptor agents on ADP (0.5 \(\mu\)mol/L)- or collagen (1.5 \(\mu\)g/mL)-induced aggregation of equine platelets in citrated plasma were plotted (Figure 3). Adrenaline, noradrenaline, and 4 \(\alpha\)-adrenoceptor agonists (xylazine, oxymetazoline, clonidine, and medetomidine) were ineffective against ADP-induced aggregation of equine platelets. Four \(\alpha\)-adrenoceptor antagonists (atipamezole, idazoxan, tolazoline, and prazosin) also were ineffective against ADP-induced aggregation of equine platelets, whereas yohimbine and phentolamine were effective at the highest concentrations evaluated. The imidazoline compound antazoline, which is devoid of \(\alpha\)-adrenergic activity, was effective at a concentration of 100 \(\mu\)mol/L against ADP-induced platelet aggregation.

In contrast with results for ADP-induced platelet aggregation, inhibitory activity by the agents was clearly evident on collagen-induced aggregation of equine platelets. Noradrenaline, xylazine, medetomidine, and oxymetazoline caused incomplete inhibition of collagen-induced aggregation of equine platelets only at the highest concentrations evaluated. The imidazoline agent antazoline (1 to 100 \(\mu\)mol/L) significantly inhibited collagen-induced platelet aggregation in a dose-dependent manner (Figure 4; Table 2). The \(\alpha\_2\)-adrenoceptor antagonists phentolamine (1 to 100 \(\mu\)mol/L), idazoxan (10 to 100 \(\mu\)mol/L), and yohimbine (10 to 100 \(\mu\)mol/L) also inhibited collagen-induced ag-
Figure 3 for remainder of key.

Figure 4—Mean±SE percentage aggregation for imidazoline and nonimidazoline α-adrenoceptor agonists (A and C) and α-adrenoceptor antagonists (B and D) on platelet aggregation induced by ADP (0.5 μmol/L; A and B) or collagen (1.5 μg/mL; C and D) in citrated equine plasma. Each mean±SE represents results for 5 animals. See Figure 3 for remainder of key.

Table 1—Mean±SE potency of imidazoline and nonimidazoline α-adrenoceptor agents for the inhibition of aggregation of bovine platelets induced by a high dose of collagen (10 μg/mL).

<table>
<thead>
<tr>
<th>Agent</th>
<th>IC_{50}</th>
<th>IC_{50}</th>
<th>IC_{50} ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline</td>
<td>0.4 ± 0.3</td>
<td>5.4 ± 3.1</td>
<td>7.7</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.7 ± 0.2</td>
<td>3.0 ± 1.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Phenotamine</td>
<td>2.3 ± 1.0</td>
<td>0.7 ± 0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Yohimbine</td>
<td>16.1 ± 8.0</td>
<td>7.5 ± 3.01</td>
<td>10.7</td>
</tr>
</tbody>
</table>

*Each value represents results for 5 animals.

Table 2—Mean±SE potency of imidazoline and nonimidazoline α-adrenoceptor agents for the inhibition of aggregation of equine platelets induced by collagen (1.5 μg/mL).

<table>
<thead>
<tr>
<th>Agent</th>
<th>IC_{50}</th>
<th>IC_{50}</th>
<th>IC_{50} ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antazoline</td>
<td>0.9 ± 0.6</td>
<td>6.3 ± 3.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>0.9 ± 0.7</td>
<td>8.3 ± 4.9</td>
<td>1.0</td>
</tr>
<tr>
<td>Yohimbine</td>
<td>1.2 ± 0.8</td>
<td>6.5 ± 4.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Idazoxan</td>
<td>2.8 ± 2.6</td>
<td>7.3 ± 4.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Oxymetazoline</td>
<td>20.0</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

*Each value represents results for 5 animals.

Discussion

The results of the study reported here confirmed and expanded on results of previous studies, which found that adrenaline alone did not induce a change in aggregation of bovine and equine platelets and did not potentiate ADP- or collagen-induced platelet aggregation. Furthermore, analysis of results of the present study also revealed that noradrenaline did not stimulate aggregation of bovine or equine platelets or potentiate the ADP- or collagen-induced aggregation of bovine and equine platelets. It can be presumed that both adrenaline and noradrenaline do not act as platelet agonists in cattle and horses.

In addition, other imidazoline or α-adrenoceptor agonists (clonidine, medetomidine, and xylazine) did not have any stimulatory or potentiating effects. Clonidine can induce, at least to a limited degree, aggregation in human platelets and can potentiate ADP-induced platelet aggregation.9 In the present study, clonidine did not potentiate ADP-induced aggregation in bovine or equine platelets, whereas oxymetazoline, an imidazoline adrenoceptor agonist, only potentiated ADP-induced aggregation in bovine platelets and had no effect on aggregation in equine platelets. In another study conducted by our research group, we found that clonidine did not potentiate ADP-induced platelet aggregation in dogs, but oxymetazoline caused a small potentiation of the ADP-induced platelet aggregation. Results of the present study, in combination with results of our previous study, highlight species-specific variation in the potentiation of platelet aggregation.

In the present study, adrenaline and the imidazoline α₂-adrenoceptor agonist clonidine had an inhibitory effect, rather than a stimulatory effect, on high-dose ADP- and high-dose collagen-induced aggregation in bovine platelets. Furthermore, the α₂-adrenoceptor antagonists phenotolamine (imidazoline) and yohimbine (nonimidazoline) also significantly inhibited collagen-induced aggregation of bovine platelets by >50%. Noradrenaline, other α-adrenoceptor agonists (xylazine, oxymetazoline, and medetomidine), and α-adrenoceptor antagonists (atipamezole, idazoxan, tolazoline, and prazosin) were less effective or ineffective in inhibiting collagen-induced aggregation of equine platelets.

The IC_{50} values obtained for the inhibition of collagen-induced aggregation of equine platelets were summarized (Table 2). The IC_{50} values were not attained for adrenaline, noradrenaline, xylazine, clonidine, medetomidine, atipamezole, tolazoline, or prazosin. The inhibitory potencies (based on the IC_{50} values) of antazoline, phenotolamine, idazoxan, and yohimbine were approximately equal for aggregation of equine platelets.

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In contrast, the imidazoline $\alpha_2$-adrenoceptor agonist oxymetazoline inhibited collagen-induced aggregation of equine platelets by > 25%. Furthermore, the imidazoline compound antazoline, which is devoid of $\alpha$-adrenergic activity, also inhibited ADP-induced aggregation of equine platelets and strongly inhibited collagen-induced aggregation of equine platelets in a dose-dependent manner. It can be presumed that in horses (as well as in cattle), these agents exert a non-adrenergic effect via a non-$\alpha_1$-adrenoceptor mechanism. The $\alpha_1$-adrenoceptor antagonist idazoxan as well as phentolamine and yohimbine clearly had inhibitory activity against collagen-induced aggregation of equine platelets. Adrenaline, noradrenaline, and the remaining $\alpha_1$-adrenoceptor agents were less effective or completely ineffective in inhibiting ADP- or collagen-induced aggregation of equine platelets. The drugs that had effects on equine platelets differed from those that had effects on bovine platelets; adrenaline and clonidine, both of which had a strong inhibitory effect on aggregation of bovine platelets, were ineffective on equine platelets. In addition, effective doses of ADP and collagen differed between platelets from cattle and horses. Analysis of these results suggests that there are critical species-specific differences (even between horses and cattle) in the platelets or in the reactivity of platelets, which had a strong inhibitory effect on aggregation of bovine platelets, were ineffective on equine platelets. In addition, effective doses of ADP and collagen differed between platelets from cattle and horses. Analysis of these results suggests that there are critical species-specific differences (even between horses and cattle) in the platelets or in the reactivity of platelets.

Mammalian platelets have a wide range of responses to adrenaline in part because adrenaline can act via excitatory $\alpha_2$-adrenoceptors and inhibitory $\beta$-adrenoceptors. Adrenaline acts as a platelet agonist in humans, with a mean receptor density of 258 $\alpha_2$-adrenoceptors/platelet and 66 $\beta$-adrenoceptors/platelet ($\alpha_2$-adrenoceptor/$\beta$-adrenoceptor ratio, 3.91). It has been suggested that the $\alpha_2$-adrenoceptor/$\beta$-adrenoceptor ratio determines whether adrenaline acts as a platelet agonist. Although data on platelet adrenoceptor density is not available for cattle and horses, it can be speculated that a 100 $\mu$mol/L dose of adrenaline in the present study stimulated $\beta$-adrenoceptors, which inhibited platelet aggregation. This does not exclude the possibility that adrenaline inhibited ADP-induced aggregation of bovine platelets in a dose-dependent manner. In the present study, certain imidazoline agents inhibited ADP- or collagen-induced aggregation of bovine or equine platelets. There is no evidence of imidazoline receptors, in addition to $\alpha_2$- and $\beta$-adrenoceptors, on bovine and equine platelets. We presume that the binding sites mediating these nonadrenoceptor effects may be the imidazoline receptors that have been identified on human platelets. Future investigations to identify and elucidate the function of these receptors is warranted. Nevertheless, it is possible that the imidazoline structure is involved, in part, in the inhibition of adrenaline-potentiated aggregation and that imidazoline adrenoceptor agents also interact with atypical nonadrenergic receptors.

A variety of drugs are clinically available that have activity at $\alpha_2$-adrenoceptors. In veterinary medicine, including bovine and equine practice, the $\alpha_2$-adrenoceptor agonists xylazine, medetomidine, and clonidine may be used for sedation, analgesia, and premedication for general anesthesia, and the $\alpha_2$-adrenoceptor antagonists atipamezole and yohimbine are used for the reversal of the effects of the $\alpha_2$-adrenoceptor agonists. In the present study, the effects of clinically used $\alpha_2$-adrenoceptor agents on aggregation of platelets from healthy cattle and horses were evaluated. In combination with pharmacokinetic data after systemic administration of xylazine and medetomidine at clinically recommended doses in cattle and horses, results for the present study indicated that the $\alpha_2$-adrenoceptor agonists xylazine and medetomidine at estimated effective blood concentrations may be used by bovine and equine practitioners without concern for adverse effects on platelet function and hemostasis.

On the other hand, clonidine may be used safely for adverse platelet reactions on hemostasis in horses because it has no stimulatory effect on equine platelets, whereas a relatively high dose of clonidine may inhibit ADP- and collagen-related hemostasis in cattle. The $\alpha_2$-adrenoceptor antagonists yohimbine and phentolamine may also have inhibitory effects on bovine and equine hemostatic systems for certain events, such as blood vessel damage and collagen exposure. Yohimbine is ineffective in antagonizing xylazine-induced sedation and has a narrow therapeutic safety margin in cattle; therefore, it is proposed that tolazoline, an imidazoline $\alpha_2$-selective antagonist, could be used in cattle as a substitute for yohimbine. In addition, the present study revealed that both tolazoline and atipamezole have no stimulatory effects on bovine and equine platelets and thus may have useful clinical applications in cattle and horses.

In the present study, adrenaline, noradrenaline, and $\alpha_2$-adrenoceptor agents alone did not induce a change in aggregation in bovine or equine platelets or potentiate platelet aggregation induced by ADP or collagen. It is suggested that the $\alpha_2$-adrenoceptors on bovine and equine platelets may not be involved in the mediation of platelet aggregation, at least when stimulated by ADP or collagen, and that nonadrenergic imidazoline receptors, similar to receptors described in human platelets, may also be present on bovine and equine platelets. Furthermore, analysis of the results of the present study revealed that clinical doses of $\alpha_2$-adrenoceptor agonists (xylazine and medetomidine) and $\alpha_2$-adrenoceptor antagonists (tolazoline and atipamezole) may be used in bovine and equine practice without concern for adverse effects on platelet function and hemostasis. Various drugs had differing efficacy on platelets of cattle and horses, and the effective doses of ADP and collagen also differed between cattle and horses. Analysis of these results suggests that there are critical species-specific differences in the platelets or in the reactivity of platelets, even between horses and cattle.

a. MCM Hema tracer 804, LMS Co Ltd, Tokyo, Japan.
b. Tokyo Kasei Industries Co, Tokyo, Japan.
c. Sigma Chemical Co, St Louis, Mo.
d. Ciba-Geigy Corp, Hyogo, Japan.
e. Farmos Group Ltd, Turku, Finland.
f. Bayer, Leverkusen, Germany.
References


