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Withdrawal Times of Intramammary Antibiotics in Camel and Cows Milk of Golestan State Iran

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Abstract: The study was conducted to determine withdrawal periods of intramammary preparations Curaclax (ampicillin+ceplulosporin), oxymast (oxytetracycline) and spectrazol (cefruxine) in camel and cow milk. Withdrawal periods in milk were 4 days in cows versus 5 days in camels for curaxlox and 4 days in cows versus 6 days in camel for oxmast and spectrazol. The significant ($p<0.05$) difference in withdrawal periods between camel and cow emphasizes the need to establish specific withdrawal periods for other drugs in the camel.

Key words: Curaclax, oxymast, camel, cow, drugs, milk

INTRODUCTION

The antibacterial treatment of mastitis in lactating animals is of considerable regulatory concern because of the possibilities of antibacterial residues in milk (Sandholm *et al*., 1990). Intramammary (imm) infusion has been recognized as the route for treating mastitis (Soback, 1988). Over 26% of milk samples collected 96 h post-treatment was positive for antibiotic residues (Berruga *et al*., 2003).

The possible presence of antibacterial residues in milk poses a risk for consumers because these may cause allergic reactions, intestinal dysbiosis or even the emergence of resistant bacteria (Dewdney *et al*., 1991). Failure to observe the correct withdrawal time was cited as the most common reason for violative drug residue levels in a study performed by the FDA in the 1970's (Bevill, 1989) and continued to be the most common cause of the residue violations in the 1990's.

The withdrawal period may be defined as the period that is required following the last medication in order to bring the concentration of the drug to below a tolerable value.

The actual withdrawal time appearing on antibiotic label is also a function of experimental design that the manufacture uses in the research studies. Such labels contain no information about withdrawal times in camels and veterinarians have to extrapolate withdrawal times of drugs for dairy camels from other species.

This is scientifically unacceptable since the camel differs in its physiological, anatomical and pharmacological characteristics from other animals (Abdalla and Abdalla, 1979; Al-Dughaym *et al*., 1998). This study was carried out to determine the withdrawal period of intramammary antibiotics in camel milk.

MATERIALS AND METHODS

Animals and treatment: About 6 majahem lactating dromedary camels and 6 jersey dairy cows were used in this study ranging in age from 4-6 years. The animals were housed in stalls and given free choice alfalfa hay and water. The entire content of the intramammary infusion syringe containing antibiotics, formulated for treatment of bovine mastitis was injected into each udder. The preparations used were oxymast (oxytetraycline, 500 mg, Bimeda, UK), curalox (amicillim 75 mg+cloxacillin 200 mg, Norbrook, UK) and spectrazol (cefuroxime 250 mg, Schering-Plough, Germany).

Collection of milk samples: Milk sampling was performed at 12 h interval. All samples were frozen immediately after they were taken. The samples were subsequently thawed and diluted 50:50 with distilled water and mixed well to reach the correct viscosity.

Antibacterial assay: Antibacterial concentration in milk was determined using an agar diffusion method with cut wells. *Bacillus stearothermophelus* (ATCC 10142) was

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used to test penicillins (Al-Nazawi and Homeida, 2005). *Bacillus subtilis* (ATCC 663) was used to test tetracyclines (Al-Nazawi and Homeida, 2002).

Statistical test: ANOVA followed by Turkey's multiple range test was used to test the data. A $p<0.05$ was considered significant.

Antibacterial screening test: The screening tests used was brilliant Black Reduction Test (BRT; AIM-An Lytik in Milch production-Und-Vertriebs UmbH; Munchen, Germany). Briefly, the test is based on detecting inhibition of the growth of spores of *Geobacillus stearothermophilus* var. *calidolactis* C. The test medium is a mixture of nutrients, test bacteria, a clored indicator (brilliant-black) and supplements.

When milk sample contains no residue or these are under the detection limits, the spores germinate and grow and their metabolic activity makes the indicator change color. In the presence of antibacterial residues, no bacterial activity will be defected and the indicator color will remain unchanged. The color change can be assessed visually or photometrically at wavelengths of 450 and 620 nm.

RESULTS AND DISCUSSION

Recently, much attention has been paid to the utilization of the inherent properties of camel milk for human health as hyperglycemic, antidiabetic, antichslesterolaemic and anticancer (Mal *et al*., 2000, 2001; Sahani *et al*., 2005). Therefore, concern over camel milk antibiotic residues are economic as well as public health related.

Table 1 shows the results of depletion of intramammary antibiotics from camel udder. The Maximum Residue Limit (MRL) and safe clearance levels for antibiotic residues in milk fixed by codex alimentrius, European Countries (EC) regulations and Unitied States food and drug administration for ampicillin, cloxacillin, cepholosporins and oxytetracycline are 4, 30, 100 and 100 mg kg^{-1}, respectively (Honkanen-Buzalski and Reybroeck, 1997). In the present experiment, the MRLs were reached after 132 h for ampicillin and cloxacillin suggesting that these periods represent the withdrawal periods for the 4 antibiotics in camel milk.

The withdrawal periods of the 4 antibiotics are significantly ($p<0.05$) longer than those in goats (Karzis *et al*., 2007), cows (Bangen *et al*., 1992; Debackere, 1995) and sheep (Sierra *et al*., 2009). Animal models of infection have shown that bacterial killing may be described as a function of either concentration or time-dependent (Sharma *et al*., 2002).

Table 1: Effect of intramammary adminstration of curaclos, oxymast and spectrazol on concentration of antibiotic in camel milk

Time (h) after antibacterial adminstration	Antibacterials: Curaclox (ampicullin)	Curaclox (cloxacillin)	Oxymast (oxytetracycline)	Spectrazol (cefruxime)
12	102.0±12.1	1225±65.0	980±44.0	8600±120.0
24	93.0±11.6	980±52.00	810±40.0	5250±110.0
26	81.0±9.10	820±44.00	720±30.0	3800±102.0
48	52.0±6.30	710±32.00	580±15.0	2100±90.00
60	36.8±5.10	605±25.00	480±14.0	1400±70.00
72	24.1±3.10	450±15.00	420±13.0	920±65.000
84	18.6±2.10	261±12.00	310±12.0	750±35.000
96	10.1±2.00	140±12.00	280±11.0	510±25.000
108	8.2±1.600	81±8.5000	210±10.0	420±18.000
120	5.1±1.200	45±6.1000	160±10.0	350±13.000
132	3.1±0.6*0	26±3.1000*	105±8.20	200±11.000
144	2.2±0.500	19±2.1000	94±8.3*	95±10.0000
156	1.6±0.200	12±2.0000	70±7.100	120±9.5000
168	1.2±0.200	9±1.50000	53±5.100	90±7.60000

*Maximum Residue Limits (MRL)

Table 2: Detection limits of brilliant reduction test in milk of camels and cows treated with intramammary antibiotics preparations

(h) after antibacterial administration	Anitbacterials curaclox (Ampicillin+ cloxacillin)		Oxymast (Oxytertracycline)		Spectrazol time (cefruxime)	
	Camel	Cow	Camel	Cow	Camel	Cow
12	+	+	+	+	+	+
24	+	+	+	+	+	+
26	+	+	+	+	+	+
48	+	+	+	+	+	+
60	+	+	+	+	+	+
72	+	+	+	+	+	+
84	+	+	+	+	+	+
96	+	-	+	-	+	+
108	+	-	+	-	+	+
120	+	-	+	-	+	+
132	-	-	+	-	+	-
144	-	-	-	-	-	-
156	-	-	-	-	-	-
168	-	-	-	-	-	-

+Indicates presences of antibodies and indicates absences of antibiotic in camel milk

Bacteriostatic antibiotics and β-lactams are time dependent. Furthermore, the camel exhibits certain characteristics that differ from other domestic animals. They have low glomerular filteration rate (Etzion and Yagil, 1985), long nephron (Abdalla and Abdalla, 1979) oval erythrocytes (Etzion and Yagil, 1985) and low drug metabolizing enzyme activities (El-Sheikh *et al*., 1986, 1991; Al-Shiekh *et al*., 1988) which are expected to delay the elimination of drugs in the camel.

The BRT results (Table 2) were negative at times and levels corresponding to MRL for the 4 antibiotics which further confirms the observation that withdrawal periods in the camel to be significantly longer than in cows. The values were 4 and 5 days for the camel for ampicillin and cloxacillin 4 days for the cow and 6 days for the camel for oxytetracyeline and cefruxime.

CONCLUSION

The ersults of this study shows that BRT has been used to detect antibiotic residues in milk of cows, sheep and goats in many places (Sierra *et al*., 2009). The difference in withdrawal periods in the camel from that in other ruminants emphasizes the need to establish newer withdrawal periods of drugs in camels.

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