Final Report

CHARACTERIZATION OF A NEW INTRAVAGINAL PROGESTERONE DEVICE FOR CAPRINES & OVINES (DICO)

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FisRep-Syntex Agreement
Fundaciba
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1st August 2006

EXECUTIVE SUMMARY

During the months of May-July 2006 a sequence of experiments were done in order to characterize a new siliconed progesterone device for intravaginal usage in small ruminants (DICO, Syntex, Buenos Aires, Argentina).
The results shows that the serum progesterone concentrations induced by the insertion of DICO in ovariectomized females (Experiment A1), as well as in females in advanced luteal fase (day 9-10 of the interestrous cycle) (Experiment B1), are not different from the ones induced by the commercially available device CIDR-G (Pharmacia & Upjhon, Hamilton, New Zeland). In addition, the interval from the device withdrawal to estrus and ovulation was very similar for both devices (DICO: 30 h and 55 h; CIDR: 35 h and 60 h; respectively). Similarly, the ovulation rate, and the size and age of the ovulatory follicle was not different between two devices.
In ovariectomized ewes (Experiment A2), the use for six days (Short-term Protocol) of a previously six-days used DICO induced lower serum progesterone concentrations than a new one. However, serum progesterone concentrations were always over 2 ng/ml during the hole period. In cyclic ewes, the use of a DICO in a Short-term Protocol (6 days) associated with a dose of PGF2 alpha given at the moment of DICO withdrawal, induced an interval to estrus and to the ovulation of 46 and 74 hours, respectively (Experiment B2). In addition, 350 IU of eCG given at the moment of DICO withdrawal resulted in an advancement of 10 hours for both estrus and ovulation (36 and 63 hours, respectively).

Edgardo Rubianes y Alejo Menchaca
1st August 2006

The experiments were done in the facilities of the Laboratory of Physiology of Reproduction Department of Physiology (PEDECIBA, Basic Sciences Development Program), Veterinary University, Lasplaces 1550, Universidad de la República, Montevideo, Uruguay. The supervision of the study was in charge of Edgardo Rubianes, MSc, PhD and Alejo Menchaca, DVM, MSc. For the scanning and bleeding, the participation of Marcela Vilariño was crucial. The hormonal determination in the blood samples was assayed by Elize Van Lier, DVM, MSc, PhD. The animal handling was performed by Federico Arruti and Milton Pintos. Financially supported by FUNDACIBA (PEDECIBA Fundation).
Edgardo Rubianes is Professor on Animal Reproduction, Facultad de Agronomía, Universidad de la República, is *senior* researcher of the PEDECIBA, of the postgraduate programs of the Agriculture Faculty and Veterinary Faculty, and is member of the National Fund of Researchers.
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CHARACTERIZATION OF A NEW INTRAVAGINAL PROGESTERONE DEVICE FOR CAPRINE AND OVINE (DICO)

Several experiments were performed using ovariectomized and cycling ewes during May to July 2006.

A) EXPERIMENTS WITH OVARIECTOMIZED EWES

A1) COMPARISON OF DICO VS. CIDR USING LONG-TERM TREATMENTS

a) **OBJECTIVE**

This study was designed to establish the serum progesterone concentration induced by a new siliconed intravaginal device (DICO, Syntex) comparing with a commercial intravaginal device. The progesterone exposure was maintained during 14 days (traditional-term treatment),. The animals did not have ovarian activity (ovariectomized ewes).

b) **ANIMAL HANDLING**

Eighteen ovariectomized Corriedale multiparous ewes which weighted 50,5 ± 4,9 kg (mean ± SD) and had a body condition score of 3,9 ± 0,3 (0 to 5 scale) were used. The females were held together in appropiate sheltered pens and were equally daily fed and handled. Animals were fed alfalfa hay (2.5 kg/day/each) and commercial pelleted concentrate (900g/day/ewe). The alfalfa hay was given in equals parts three times a day: at 9 AM; at 1 PM and at 6 PM, and the concentrate was given one hour later. The females received this management from two month before the experiments

c) **DEVICES**

The animals were divided in two experimental groups (n=9), treated with DICO and CIDR-G during 14 days. Both intravaginal devices contain 0,3 gr of progesterone. The evaluated intravaginal device was produced by SYNTEX in april 2006. The commercial intravaginal device was CIDR-G (Controlled Internal Drug Release, Eazi-Breed, Auckland, Nueva Zeland) suitable for ewes and goats (Pharmacia & Upjohn; batch N^{o} F111042; expiry date: 11/2007).

e) **BLOOD SAMPLES AND PROCESSING**

Daily blood samples were obtained by jugular venipuncture by the same technician. The samples were taken from 8 to 9 AM (i.e. before the animals were fed) and the exception to this rule only took place when more than one sample was taken (between Day 0 and Day 1, and between Day 14 and Day 16, relative to device insertion). Glass tubes were filled with blood samples, left to clot at room temperature and centrifugated at 3000 rpm for 15 minutes within one hour after collection. Serum was separated using syringe and needle. Duplicated serum aliquots were stored in 1.5 ml eppendorf tubes properly identified. Then, the tubes were immediately stored in a freezer at -20 ^{o}C and kept there until their processing for the determination of serum progesterone by radioimmunoassay (RIA).

f) **DETERMINATION OF SERUM PROGESTERONE BY RIA**

The serum progesterone concentration was determined in duplicate samples using a commercial Kit of direct solid-phase Radioimmunoassay Iodo^{125} (Coat-a-Count, DPC, Los Angeles, CA, USA), previously validated for ovine serum by Garófalo & Tasende, (1996).. According to the manufacturer, the antibody against progesterone is highly specific for progesterone with a particularly low cross reactivity to other natural steroids. The average control values were of 0,75 ng/ml, 2,77 ng/ml and 8,57 ng/ml for low, medium and high values, respectively. The coefficient of variation intra-assay were 8%, 6,8% and 4,6% respectively, and the inter-assay were 10,5%, 9% and 8,2%. The analytical detection limit of the assay was 0,12 ng/ml.

g) **STATISTICAL STUDIES**

The data for the concentrations of progesterone were studied using the mixed model of the Statically Analysis System (SAS). The model included the group and time effect and their interaction.

h) **RESULTS**

The results show that the serum progesterone concentration induced by the insertion of a CIDR or a DICO were similar (P> 0,1). Progesterone levels were not different neither during the 14-day treatment period (Figure1), nor immediately after their insertion (Figure 2a) and their withdrawal (Figure 2b).

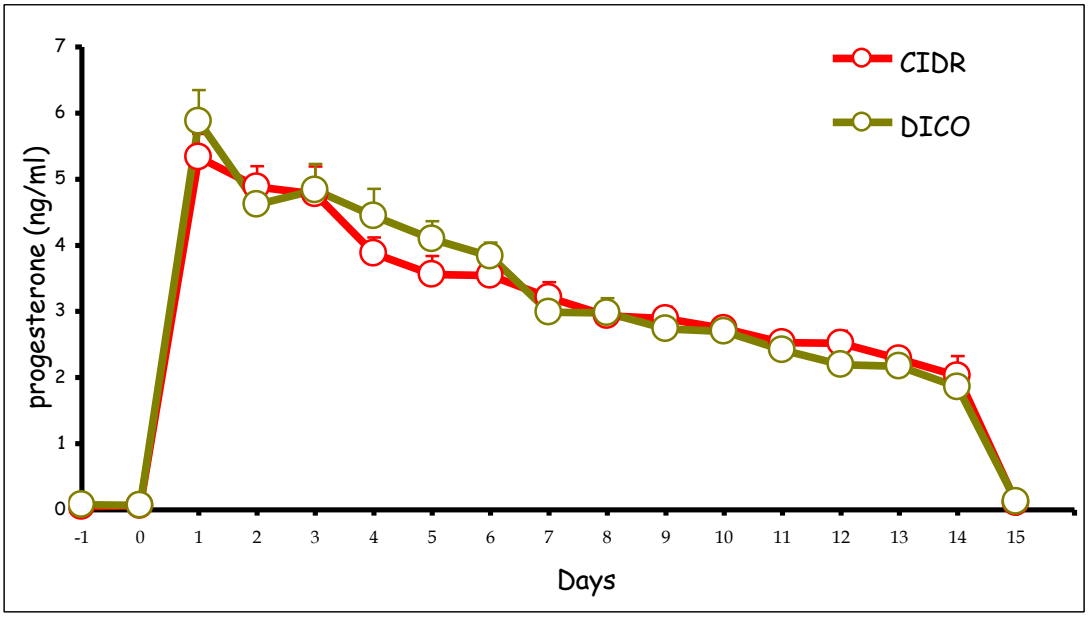
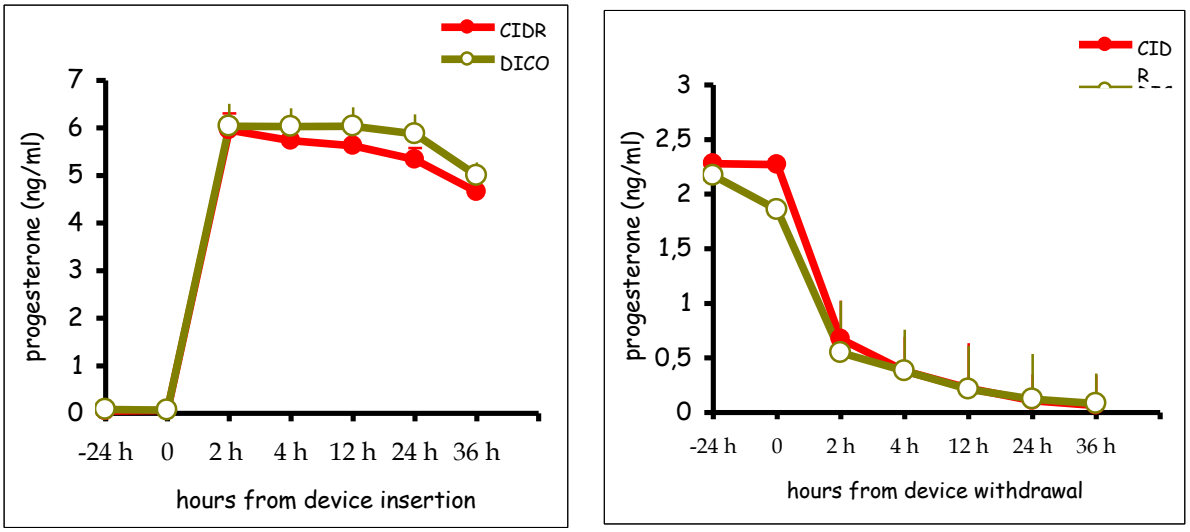


Figure 1. Serum progesterone concentrations (Mean ± SEM) induced with a new intravaginal progesterone device DICO (Syntex; n=9) compared with CIDR (n=9) in ovariectomized ewes. Day 0 is the moment when the device was inserted and Day 14 is the moment when the device was removed.

Figure2. Serum progesterone concentrations (Mean ± SEM) induced with a new intravaginal progesterone device DICO (Syntex; n=9) compared with CIDR (n=9) in ovariectomized ewes.



Progesterone concentrations soon after device insertion or device withdrawal are depicted in A and B, respectively.

h) **CONCLUSION**

Serum progesterone concentrations were similar using DICO or CIDR for 14 days. Therefore, we can use DICO with the same effectiveness of the CIDR to control the serum progesterone concentrations in ewes.

A2) COMPARISION BETWEEN A NEW DICO DEVICE WITH A REUSED ONE

a) **OBJECTIVE**

The objective was to determine, the serum progesterone profiles induced by a DICO inserted for six days, comparing with the reuse of a DICO previously used for six days.

b) **ANIMALS AND TREATMENTS**

Eleven ovariectomized Corriedale adult ewes, which weighted 50,8 ± 4,8 kg (mean ± Dst) and had a body condition score of 3,9 ± 0,1, were used. The experiment was done in two crossed replicates. Six females received a new device in the first replicate, and in the second replicate received a previously six-day-used device. On the opposite, the other five females received a six-day-used device in the first replicate and in the second replicate a new device was placed. The interval between two replicates was 7 days.

The animal handling, taking and processing of blood samples, and the serum progesterone determinations by RIA were done as described in literals A1d, A1e and A1f.

c) **RESULTS**

Figure 3 shows the serum progesterone concentrations. The insertion of a previously used DICO induced significantly lower progesterone concentrations during all the period. However, is interesting to observe that those are more stable in connection with time than when a new DICO was used. What is more, in both groups the concentrations were maintained up to 2 ng/ml and were stable during all the period.

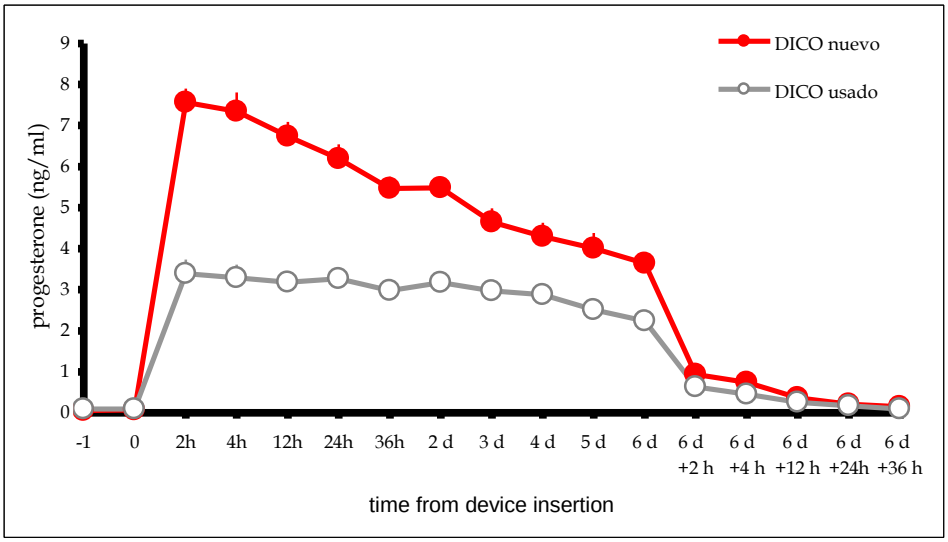


Figure 3. Serum progesterone concentration (Mean ± SEM) of 11 ovariectomized ewes treated by six days with a new or previously six-day-used progesterone intravaginal device DICO (Syntex). Day 0 is the moment of device insertion and Day 6 is the moment of device withdrawal.

d) **CONCLUSION**

The use of a DICO previously used by 6 days allows to obtain adequate concentrations of serum progesterone (> 2 ng/ml) during all the treatment. Therefore, with a Short-term protocol for six days is possible to reuse the DICO device previously used for six days.

B) EXPERIMENTS WITH CYCLING EWES (in advanced luteal phase: days 9-10)

B1) COMPARISION BETWEEN DICO AND CIDR DEVICES IN LONG-TERM TREATMENTS

a) **OBJECTIVES**

The objective was to characterize the serum progesterone profiles induced by the new designed device (DICO) with a treatment of traditional length (14 days) and compare them with the commercial available device (CIDR), using cycling animals (i. e. on the normal conditions of usage of this product).

We determined the follicular development and the grade of synchronization of the ovulatory moment using the traditional length treatment (14 days).

b) **ANIMALS**

Fifteen adult Corriedale ewes were used in two groups: CIDR group (n= 7) and DICO group (n= 8). The animals weighted 43,8 ± 4,3 kg. and had a body condition score of 4,0 ± 0,2.

c) **ANIMAL HANDLING**

The animals were kept together in appropriate shelter pens, receiving the same food and daily handling. The food consisted in alfalfa hay (2,5 kg/day/each) and commercial pelleted concentrate (900g/day/each) . The alfalfa hay was given in equals parts three times a day: at 9 AM; at 1 PM and at 6 PM. The concentrate was given one hour later.

d) **EXPERIMENTAL TREATMENTS**

With the objective to initiate the experiment in an advanced luteal phase (day 9-10 of the estrous cycle), the estrous cycles was previously synchronized using two doses of PGF2 alpha analogue (75µg each dose, D cloprostenol, Ciclase, Syntex, Argentina) separated for 7 days. Estrous behavior was checked with two crayon-harnessed androgenized wethers (3 consecutive doses separated by 7 days of 200 mg of ciclopentilpropionato of testosterone, Dispert Laboratory, Uruguay). The marker wethers were located with the ewes (one per each experimental group), and were rotated every 6 hours between both groups. Signs indicating heat were registered every 6 hours during the 120 hours following the device withdrawal.

e) **OBTENTION AND PROCESSING OF BLOOD SAMPLES**

The samples were obtained and processed as described in A1e and A1f.

f) **OVARIAN ULTRASONOGRAPHY MONITORING**

Ovarian ultrasonography was performed once a day from 3 days before the device insertion until the day of device removal, and then, twice a day until the ovulation was detected and confirmed in the next scan.

Ultrasonographic examinations were done with an Aloka 500 equipment provided with a transducer of 7.5 MHz used by transrectal via according to Rubianes et al. (1997). The acting technicians have a great experience in this technique and the animals rapidly get used to this procedure which is totally innocuous.

After soon the ovaries were located, a scanning of the observed structures was done (follicles > 2 mm and the corpora lutea (CL)). The diameter of the follicles and the diameter of the CL were measured using the scanning monitor caliper.

The analysis of the obtained information allowed to determine different variables related to the follicles dynamic such as the characteristics of the follicular waves, follicle ovulatory size and the moment of ovulation. Data were compared by Analysis of Variance (ANOVA).

g) **RESULTS**

The figure 4 shows the progesterone serum concentrations during the treatment days in both experimental groups. The results showed that the DICO maintained very similar values to those obtained with a CIDR in cycling ewes, in a similar way to that founded in the previous experiment with ovariectomized ewes.

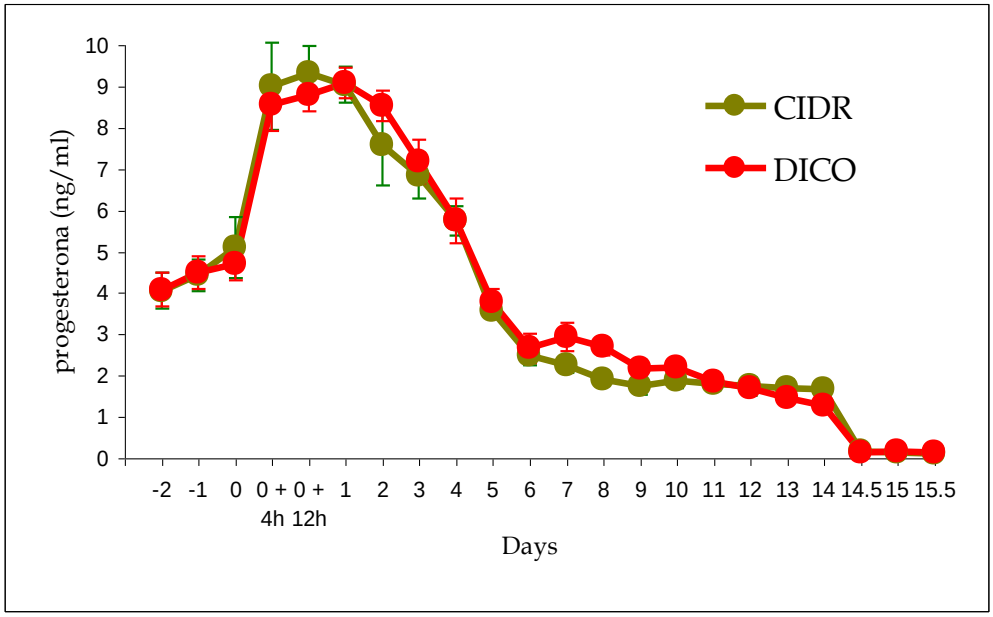


Figure 4. Serum progesterone concentrations (Mean ± SEM) induced with a new intravaginal device (DICO) compared with a CIDR-G in cyclic ewes treated during 14 days. Day 0 is the moment of device insertion and Day 14 is the moment of device withdrawal.

Table 1 shows that the onset of estrus, the follicle development and the ovulatory moment induced by a treatment with DICO, were very similar to the results obtained with CIDR. This trial shows that both devices used during 14 days induce the same response in cyclic ewes.

Tabla 1. Characteristics of the ovulatory follicle induced by a new intravaginal progesterone device (DICO) placed during 14 days in cyclic ewes compared with a CIDR-G.

	Onset of estrus (h)*	Moment of ovulation (h)*	Ovulation rate	Diameter (mm) at ovulation	Lifespan (days) of ovulatory follicle
DICO	34,5 ± 2,8	60,0 ± 9,1	1,3 ± 0,5	7,0 ± 0,8	8,6 ± 2,2
CIDR	30,0 ± 7,7	54,9 ± 6,4	1,4 ± 0,5	7,3 ± 1,1	10,0 ± 2,9
P=	0,15	0,23	0,50	0,52	0,32

*hours from device withdrawal

h) **CONCLUSION**

The present study demonstrate that serum progesterone concentration, the onset of estrus and the ovulatory moment induced by a DICO are very similar than the results obtained with a CIDR. Serum progesterone concentrations maintain the same values for both devices during the whole treatment and the ovulatory moment ocurred approximately 55-60 hours after the device withdrawal.

B2) SHORT-TERM PROTOCOL USING A DICO

a) **OBJECTIVE**

The objective was to evaluate the ovarian response to a Short-term Protocol (described by Rubianes & Menchaca, 2003) using a DICO. Short-term Protocol consists in 6 days of progesterone exposure associated with eCG (equine chorionic gonadotrophin) as an alternative to synchronize the ovulation and allow, in this way, the possible application of Fixed-Time Artificial Insemination (FTAI) programs.

b) **ANIMALS**

Fifteen adult Corriedale ewes with 41,9 ± 3,6 kg of live weight and a body condition score of 3,8 ± 0,6 were used. Animal handling was the same that described on the literals B1c.

c) **EXPERIMENTAL TREATMENTS**

The estrous cycle was pre-synchronized and the presence of estrus was evaluated using the same methodology described on literal B1d. One experimental group (DICO, n=7) received a Short-term Protocol for 6 days of progesterone exposure plus one dose of PGF2 alpha (75µg, D(+)cloprostenol, Ciclase, Syntex, Argentina) given at the moment of the device withdrawal.

d) **OBTENTION AND PROCESSING OF BLOOD SAMPLES**

The samples were obtained and processed as described in A1e and A1f.

e) **OVARIAN ULTRASONOGRAPHY MONITORING**

Ovarian follicular dynamics and the ovulatory follicle development were evaluated in agreement to the methodology described on the literal B1f.

f) **RESULTS**

Table 2 shows that the ovulatory moment induced by a Short-term Protocol with DICO associated to eCG induced an advance in the ovulatory moment compared to the ewes which did not receive eCG. Similarly, the onset of estrus occurred earlier in the ewes treated with eCG.

Table 2. Effect of eCG on characteristics of ovulatory follicle induced by new intravaginal progesterone device (DICO) inserted during 6 days in a Short-term Protocol in cyclic ewes.

	Onset of estrus (h)*	Moment of ovulation (h)*	Ovulation rate	Diameter (mm) at ovulation	Lifespan (days) of ovulatory follicle
DICO	46,3 ± 5,7[a]	73,7 ± 4,5[a]	1,1 ± 0,4[a]	6,3 ± 0,4[a]	5,8 ± 0,7[a]
DICO+eCG	36,0 ± 6,4[b]	63,0 ± 5,3[b]	1,1 ± 0,4[a]	6,5 ± 0,8[a]	7,2 ± 1,9[a]

*hours from device withdrawal. Columns with different superscript differ. a vs b: P< 0,01.

Figure 5 shows serum progesterone concentrations in both groups. As it was expected, both groups showed very similar serum progesterone concentrations due to the fact that the treatment was the same until the device withdrawal.

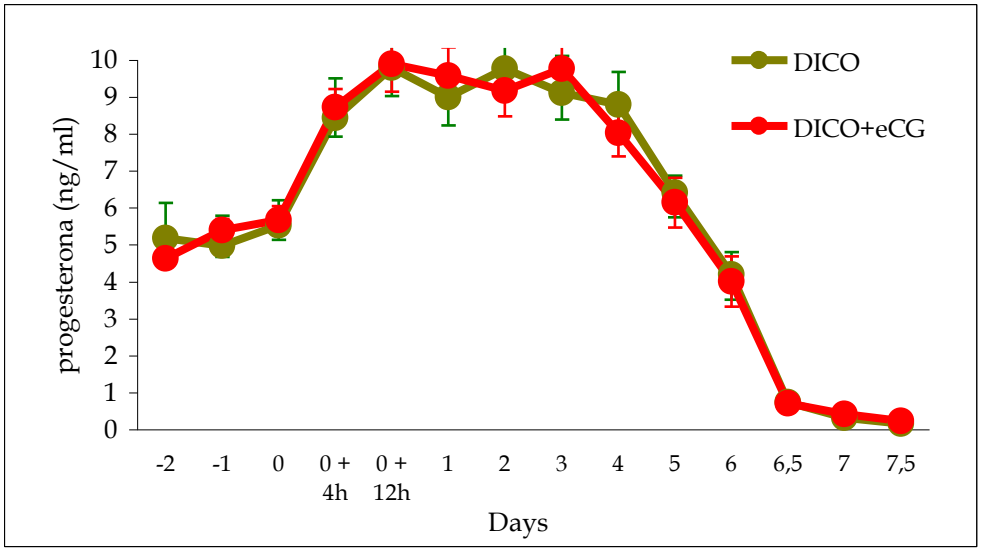


Figure 5. Serum progesterone concentrations in cyclic ewes treated for six days with a intravaginal progesterone device (DICO). Day 0 is the moment of device withdrawal. At the moment of device withdrawal every animal received a dose of PGF2 alpha and one group recieved a dose of eCG (DICO+eCG group).

g) CONCLUSION

The use of eCG associated to the Short-term Protocol with a DICO induced an advancement in the onset of estrus as well as in the ovulatory moment in cyclic ewes. The estrus was induced at 36 hours and the ovulation at 63 hours after DICO removal/eCG administration.

References

Garófalo E; Tasende C. 1996. Uterine oestrogen and progesterone receptors in prepubertal ewes: distribution in myometrium, endometrium and caruncles. Veterinary Research 27:177-183.

Rubianes E, Beard A, Dierschke D, Bartlewski P, Adams GA, Rawlings NC, 1997. Endocrine and ultrasound evaluation of the response to PGF 2 alpha and GnRH given at different stages of the luteal phase in cyclic ewes. Theriogenology 48:1093-1104.

Rubianes E; Menchaca A. 2003. The pattern and manipulation of ovarian follicular growth in goats. Animal Reproduction Science 78:271-287.

Serum progesterone concentrations after insertion of a new intravaginal device (DICO) in ovariectomized ewes

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A new intravaginal device of silicone containing 0.3 g of progesterone for use in sheep (DICO, Syntex, Buenos Aires, Argentina) is currently being developed. A study was conducted in ovariectomized ewes to compare the serum progesterone concentrations induced after the insertion of a DICO with those induced by a commercial available silicone device (CIDR-G, Pharmacia & Upjohn; batch F111042, Auckland, New Zealand). Both devices contained equal amounts of progesterone. Eighteen ovariectomized adult Corriedale ewes were used and allocated in two groups (n=9 each). The ewes weighed 50.5 ± 1.2 kg (Mean SEM) and had a body condition of 3.9 ± 0.1 (scale 0= emaciated to 5= fat). Animals were fed alfalfa hay (2.5 kg/day/each) plus pellets containing oats, barley and wheat (900 g/day/each) three times daily (9 AM, 1 PM and 6 PM). Early morning (8 AM) daily blood samples were obtained by jugular venipuncture from Day –1 to Day 16 (Day 0: device insertion; Day 14: device withdrawal). Additional samples were taken 2h, 4h, 12h and 36h after device insertion and after device withdrawal. Serum progesterone concentrations were determined by radioimmunoanalysis in duplicate using a commercial kit (Coat-a-Count, DPC, Los Angeles, CA, USA) previously validated for sheep. The intra-assay coefficients of variation for low (0.75 ng/ml), medium (2.77 ng/ml) and high (8.57 ng/ml) controls were 8%, 6.8% and 4.6%, respectively; and the inter-assay coefficients of variation were 10.5%, 9% and 8.2%, respectively. The analytical detection limit of the assay was 0.12 ng/ml. Statistical analysis was carried out using the mixed procedure of the SAS package. Figures 1 and 2 show progesterone profiles in both groups. Serum progesterone concentrations did not differ between groups (P>0.1). Both intravaginal devices induced similar progesterone concentrations throughout the 14 days period. At time of device insertion a similar sharp increase of progesterone concentrations occurred, and after device withdrawal a rapid decrease was observed. In summary, the new intravaginal device DICO induced very similar serum progesterone concentrations than CIDR-G in ovariectomized ewes.

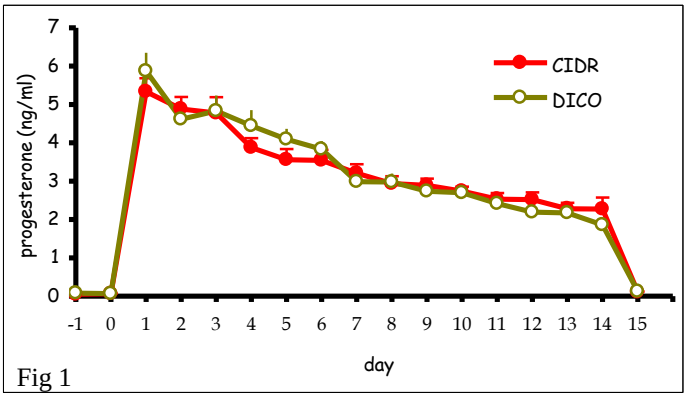

Fig 1

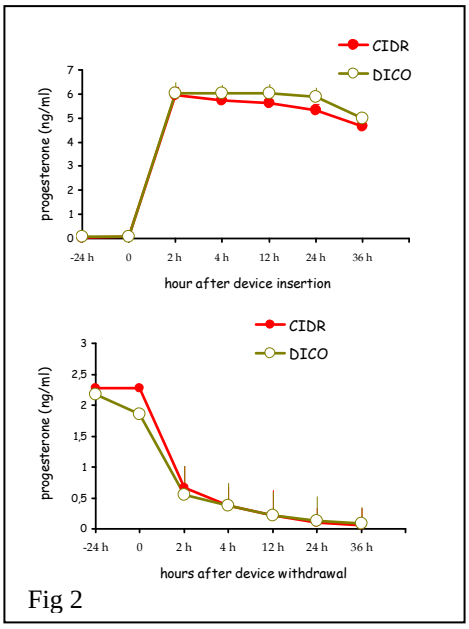

Fig 2

Supported by SYNTEX-FisRep agreement (Fundaciba).

Effect of eCG to synchronize ovulation in a Short-term Protocol using the new progesterone intravaginal device DICO in ewes

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The use of a new intravaginal device of silicone containing 0.3 g of progesterone to synchronize ovulation in sheep (DICO, Syntex, Buenos Aires, Argentina) allows similar results than the CIDR-G (data presented in other abstract). The present study evaluated the growth of the ovulatory follicle and serum progesterone concentrations induced by DICO in a Short-term Protocol in cyclic Corriedale ewes. Short-term Protocol consisted in 6 days of progesterone exposure and one dose of prostaglandin F2α (75μg of D cloprostenol, Ciclase, Syntex, Buenos Aires, Argentina) given at the time of device withdrawal (DICO group, n= 8). Another group received the same Short-term Protocol plus 350 IU of eCG (Novormon, Syntex, Buenos Aires, Argentina) at the time of device withdrawal (DICO+eCG group, n=8). Ewes were between 9 to 10 days post-estrus when the device was inserted (Day 0). Estrous behavior was checked using androgenized wethers every 6 hours during the following 120 hours after device withdrawal. Follicular development was asessed by transrectal ultrasonography (Aloka 500, 7,5 MHz), performed once a day from Day -3 until device withdrawal (Day 6) and twice a day until ovulation. Ovulation was defined as the moment of disappearance of at least one large follicle (≥ 5mm). Progesterone serum concentrations were assayed by RIA in duplicate from samples taken once a day from Day -2 until Day 6, at 0 and 12 hours from device insertion, and every 12 hours from device withdrawal during the next 36 hours. Data were compared by ANOVA. Development of ovulatory follicule is shown in Table 1. Serum progesterone concentration did not differ between groups (P> 0.1), since the treatment was the same until device withdrawal (data were pooled). At Day 0 progesterone concentration was 5.6 ± 0.4 ng/ml and increased at 4 hours (8.6 ± 0.5 ng/ml; P< 0.001) and at 12 hours (9,9 ± 0.7 ng/ml; P< 0.01) after device insertion, then began to fall at Day 4 (8.4 ± 0.5 ng/ml; P< 0.05) and fell soon after DICO withdrawal (Day 6: 4.1 ± 0.4 ng/ml; Day 6.5: 0.7 ± 0.2 ng/ml; P< 0.001).

Table 1. Effect of eCG on characteristics of ovulatory follicle induced by new intravaginal progesterone device (DICO) inserted during 6 days in a Short-term Protocol in cyclic ewes.

	Onset of estrus (h)	Moment of ovulation (h)	Ovulation rate	Diameter (mm) at ovulation	Lifespan (days) of ovulatory follicle
DICO	46,3 ± 5,7[a]	73,7 ± 4,5[a]	1,1 ± 0,4[a]	6,3 ± 0,4[a]	5,8 ± 0,7[a]
DICO+eCG	36,0 ± 6,4[b]	63,0 ± 5,3[b]	1,1 ± 0,4[a]	6,5 ± 0,8[a]	7,2 ± 1,9[a]

For different superscript, P< 0.01.

In summary, 350 UI of eCG associated with a progesterone treatment for 6 days (Short-term Protocol) using a DICO was effective to advance the onset of estrus and the moment of ovulation in cyclic ewes. This result has practical implications for timed artificial insemination programs using Short-term Protocol in sheep.

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New intravaginal progesterone device for ovarian control in ewes (DICO): moment of ovulation and serum progesterone concentrations

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A new intravaginal device of silicone containing 0.3 g of progesterone to synchronize the ovulation in sheep (DICO, Syntex, Argentina) was evaluated. We determined the growth of ovulatory follicle and serum progesterone concentrations induced by the insertion of DICO during 14 days in cyclic Corriedale ewes (n=8). Control group (n=7) was treated with a CIDR-G (0,3 g progesterone, Eazi Breed, InterAg, Hamilton, New Zealand). At the time of device insertion (Day 0) all of the ewes were between 9 to 10 days post-estrus. Follicular development was determined by transrectal ultrasonography (Aloka 500, 7,5 MHz) once a day from Day -3 until device withdrawal (Day 14) and twice a day until ovulation. Ovulation was defined as the moment of disappearance of at least one follicle ≥ 5mm. Estrous behavior was checked every 6 hours during the 120 hours following device withdrawal. Blood samples to measure progesterone concentrations were taken once a day from Day -2 until Day 14, at 0, 4 and 12 hours from device insertion, and every 12 hours from device withdrawal until ovulation, and were assayed by RIA in duplicate. Data were compared by ANOVA.

Table 1. Characteristics of the ovulatory follicle induced by a new intravaginal progesterone device (DICO) placed during 14 days in cyclic ewes, compared with a CIDR-G.

	Onset of estrus (h)*	Moment of ovulation (h)*	Ovulation rate	Diameter (mm) at ovulation	Lifespan (days) of ovulatory follicle
DICO	34,5 ± 2,8	60,0 ± 9,1	1,3 ± 0,5	7,0 ± 0,8	8,6 ± 2,2
CIDR	30,0 ± 7,7	54,9 ± 6,4	1,4 ± 0,5	7,3 ± 1,1	10,0 ± 2,9
P=	0,147	0,234	0,500	0,516	0,315

*hours from device withdrawal.

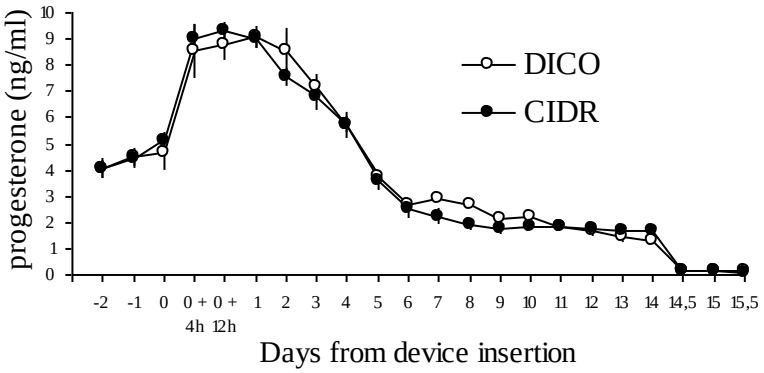

Figure 1. Serum progesterone concentrations (Mean ± SEM) induced with a new intravaginal device (DICO, n=8) compared with a CIDR-G (n=7) in cyclic ewes. Data do not differ between groups (P> 0.1).

The new intravaginal device DICO was as effective as CIDR-G to synchronize estrus and ovulation. Serum progesterone concentrations did not differ between groups. In summary, this study demonstrates the effectiveness of DICO to control ovarian activity in cyclic ewes.

Supported by SYNTEX-FisRep (Fundaciba) agreement.