Dilapan-S®

Summary of Supporting Evidence for the Use of Dilapan-S®

For Cervical Ripening Before the Induction of Term Labor

medicem

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ORIGINAL RESEARCH PUBLICATIONS

1 A randomized controlled trial of Dilapan-S vs Foley balloon for preinduction cervical ripening (DILAFOL trial)

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PUBLICATION:
American Journal of Obstetrics & Gynecology. 2019;220(3):275.e1-275.e9. doi:10.1016/j.ajog.2019.01.008

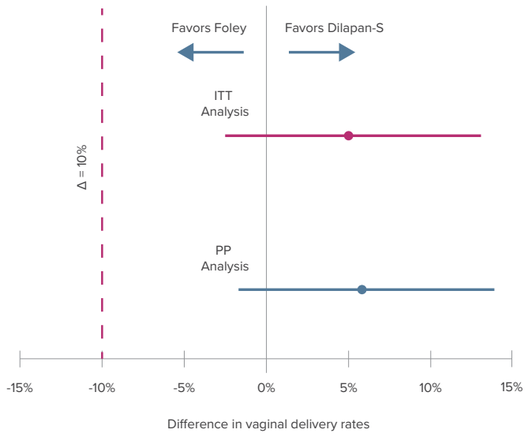
PURPOSE:
The objective of this study was to test the hypothesis that Dilapan-S is not inferior to the Foley balloon for preinduction cervical ripening during term labor induction. Dilapan-S, a hygroscopic cervical dilator made from a patented hydrogel (Aquacryl®), was cleared by the Food and Drug Administration (FDA) for cervical ripening in 2015. The Dilapan-S rods are inserted into the cervical canal, are contained within the vagina, and do not require tension. Dilapan-S works by absorbing fluid from cervical canal cells, resulting in reversible cell membrane dehydration and softening. In addition, the increase in the rod's volume creates a mechanical stretch and leads to the release of endogenous prostaglandins, causing cervical ripening. The Foley balloon, the most commonly used mechanical cervical ripening method in the United States, is inserted beyond the internal os and inflated with 30-60 mL of saline, protrudes from the introitus, and is kept under tension.

METHODS:
This was a single-center, randomized, open-label trial comparing as many Dilapan-S 4x65 mm rods that will fit into the cervical canal (without undue force) to the Foley balloon catheter filled with 60 mL of sterile saline. The study evaluated pregnant women ≥37 weeks' gestation with an unfavorable cervix (≤3 cm dilated and ≤60% effaced) and no prior uterine scar. All patients received a 20-minute cardiotocograph (CTG) monitoring before and after either device placement. Dilapan-S rods were left in place for at least 12 hours but no longer than 24 hours. The Foley was left in place for at least 12 hours. A second round with either device was used if the cervix remained unfavorable. Oxytocin was started if the cervix was ripe (≥3 cm and ≥60% effacement) and labor had not started. All patients remained in hospital but could ambulate, shower, and perform regular activity. Patients completed a satisfaction survey after insertion and postpartum. Sample size was based on a noninferiority margin of 10%, 90% power, and an estimated frequency of vaginal delivery of 71% in Foley balloon and 76% in Dilapan-S groups.

1 A randomized controlled trial of Dilapan-S vs Foley balloon for preinduction cervical ripening (DILAFOL trial)

RESULTS:
From November 2016 through February 2018, 419 women were randomized (210 to Dilapan-S with a median 5 rods inserted; 209 to Foley balloon). In the intent-to-treat analysis, the primary outcome of vaginal delivery was more common in Dilapan-S vs Foley balloon (81.3% vs 76.1%), with an absolute difference of 5.2% (95% confidence interval, -2.7% to 13.0%) indicating noninferiority for the prespecified margin **(See Figure 1)**. The difference was not large enough to show superiority. Noninferiority was confirmed in the per-protocol population (n=188 in Dilapan-S, n=204 in the Foley balloon) supporting the robustness of the results. A priori interaction analyses showed no difference in the effect on vaginal delivery by cervical dilation at randomization, parity, or body mass index >30 kg/m^2.

Figure 1: Vaginal delivery rate for Dilapan-S was noninferior to Foley balloon



Absolute difference in vaginal delivery rate (with 95% CI) between Dilapan-S and Foley balloon in the ITT (intent-to-treat) and PP (per-protocol) analysis: The 95% CI spans zero but lies wholly above the Δ margin, indicating noninferiority.

There was no significant difference in the following secondary outcomes: Change in Bishop score, operative vaginal delivery, cesarean delivery, time to active stage of labor (defined as time to cervical dilation >5 cm) **(See Table 1)**, induction to delivery time (defined as pharmacologic agent initiation to delivery), device placement to delivery time, hospital stay, regional anesthesia, analgesia during cervical ripening. The average time Dilapan-S remained in place, 12.9 hours (774.1 ± 295 minutes), was longer than the Foley group, 11.1 hours (666 ± 319 minutes; *P*=.0005). Patients in Dilapan-S group were more satisfied than patients in Foley group in terms of sleep (*P*=.01), relaxing time (*P*=.001), and performance of desired daily activities (*P*=.001). No significant difference in safety outcomes between groups was observed **(See Table 2)**.

1 A randomized controlled trial of Dilapan-S vs Foley balloon for preinduction cervical ripening (DILAFOL trial)

Table 1: Secondary outcomes according to trial group (intent-to-treat analysis)

Outcome		Treatment group		
		FB (n=209)	DS (n=208)	*P* value[a]
Change in Bishop score		3 [-3 to 9]	2 [-2 to 11]	.73
Second round of mechanical dilator		21 [9.8]	26 [13.1]	.35
Time to active stage of labor (minutes)[b]		1011 [913-1074]	1152 [1092-1205]	.21
Induction to delivery (minutes)		565 [495-634]	678 [557-734]	.64
Device placement to delivery (minutes)		1291 [1203-1408]	1441 [1343-1521]	.14
Hospital stay (hours)		63 [59-67]	66 [64-69]	.67
Total time device in place (minutes)		666 ± 319	774.1 ± 295	.0005
Indications for cesarean delivery	Nonreassuring fetal heart rate	13 (6.2)	16 (7.7)	.55
	Failure to progress	30 (14.4)	20 (9.6)	.13
	Maternal request	7 (3.3)	1 (0.5)	.03
	Other	4 (1.9)	6 (2.9)	.51
Regional anesthesia		188 (90.0)	174 (83.7)	.05
Analgesia during cervical ripening		38 (18.2)	34 (16.7)	.70

Data are represented as n (percentage), median [range], or mean ± SD.
DS, Dilapan-S; FB, Foley balloon.
[a] χ^2 or Mann-Whitney rank sum as appropriate; [b] Defined as cervical dilation >5 cm.
Saad et al. Noninferiority trial of Dilapan-S vs Foley balloon for labor induction. Am J Obstet Gynecol. 2019.

1 A randomized controlled trial of Dilapan-S vs Foley balloon for preinduction cervical ripening (DILAFOL trial)

Table 2: Safety outcomes were not different between Dilapan-S and Foley groups

Safety outcomes No statistical difference was found between groups for all outcomes ($P<.05$)	**Dilapan-S (n=196)**	**Foley (n=214)**
Uterine tachysystole[a]	0 (0)	0 (0)
Vaginal bleeding[a]	6 (3.1)	2 (0.9)
Rupture of membranes[a]	1 (0.9)	2 (0.9)
Cervical laceration[a]	2 (1)	1 (0.5)
Nonreassuring fetal status[a]	1 (0.5)	3 (1.4)
5-minute Apgar score <7	1 (0.5)	1 (0.5)
Arterial cord blood gas pH <7.1	3 (1.2)	3 (1.9)
High level of neonatal care[b]	11 (5.6)	15 (7)
Maternal infectious comorbidity (occurring within 2 weeks of delivery. None were attributable to device used.)	28 (14.3)	28 (13.1)

[a] During cervical ripening interval.
[b] Admission to higher level than normal neonatal care.

INVESTIGATOR CONCLUSIONS: Dilapan-S is not inferior to the Foley balloon for preinduction cervical ripening at term. Advantages of Dilapan-S over Foley include Food and Drug Administration approval, safe profile, no protrusion from the introitus, no need to keep under tension, and better patient satisfaction.

2 Synthetic osmotic dilators in the induction of labour – an international multicentre observational study

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PUBLICATION:
European Journal of Obstetrics & Gynecology and Reproductive Biology. 2018;229:70-75. doi:10.1016/j.ejogrb.2018.08.004

PURPOSE:
The objective of this study was to evaluate the effects of synthetic osmotic dilators (Dilapan-S/Dilasoft) in women who required induction of labor in a large prospective, multicenter, international, observational study in 7 countries including 2 U.S. sites. Two types of synthetic osmotic dilators were used: Dilapan-S (n=276) and Dilasoft (n=168) which have the same composition of patented AQUACRYL hydrogel and same mechanism of action, and Dilapan-S was the name used to report combined data for both types in this publication.

METHODS:
This was a non-interventional, observational study of pregnant women 37+ weeks of gestation that required cervical ripening during induction of labor. Primary outcomes were duration of Dilapan-S insertion (hours), total induction to delivery interval (hours), and the rate of vaginal deliveries within 24 hours. Secondary outcomes were the number of Dilapan-S dilators (rods) inserted, Bishop score increase after removal, and safety outcomes. Up to 5 Dilapan-S rods were inserted for up to 24 hours. The study included 20-minute CTG monitoring pre/post insertion.

RESULTS:
A total of 444 women, including 41 with history of cesarean delivery, had a mean of 3.8 (±1.1) of Dilapan-S rods inserted. Only 7% of participants required additional use of prostaglandins simultaneously with the action of Dilapan-S in situ.The mean duration for Dilapan-S insertion was 15.4 ± 4.9 hours. The overall rate of vaginal delivery (n=444) was 69.8%. The VBAC rate was 51.2% (21/41). No further induction method after cervical ripening was used in 15.8% (70/444) and, of these patients, 10.1% (45/444) delivered vaginally. Delivery rate outcomes were stratified according to a sub-group analysis with a cohort of less than 12 hours use [42.3% (n=188)] and more than the 12-hour time interval [57.6% (n=256)] **(See Table 1)**.

Note: Dilasoft is not cleared for use in the United States.

2 Synthetic osmotic dilators in the induction of labour – an international multicentre observational study

Table 1: Summary of delivery outcomes with Dilapan-S use <12 hours (n=188) and >12 hours (n=256)

Summary of primary and secondary outcomes	Dilator use <12 hours (n=188)	Dilator use >12 hours (n=256)	Statistical *P* value
Mean gain in Bishop score	3.6 (±2.3)	3.7 (±2.2)	.833
Mean overall vaginal deliveries	76.6%	64.8%	.0077
Mean vaginal delivery rate, 24 hours	45.7%	16%	<.0001
Mean vaginal delivery rate, 36 hours	66%	48.4%	.0002
Mean vaginal delivery rate, 48 hours	75.5%	54.7%	<.0001
Mean insertion-delivery interval (hours)	24.3 (±10.4)	39.1% (±29.2)	<.0001

At baseline, 91.4% had an unfavorable baseline Bishop score [mean of 2.9 (±1.2)], which increased to a mean of 6.5 (±2.3) after the cervical ripening period. The mean gain in the Bishop score was +3.6 (±2.3) and constantly increased across all participant cohorts. Dilapan-S was used in a broad variety of patient types: Of 444 women, 65.1% of participants were nulliparous and 34.9% were multiparous, including 9.2% with one previous cesarean section.

The indications for the induction of labor included post-term, fetal growth restriction, +/- oligohydramnios, pre-eclampsia, diabetes, renal disease, asthma, and previous cesarean section. In total, 3.4% of women experienced non-serious complications. Both maternal infection rate (3.2%) and adverse neonatal outcomes were not attributable to the use of Dilapan-S **(See Table 2)**.

In total, 3.4% of women experienced non-serious complications such as: bleeding during Dilapan-S insertion/removal (2.7%), cramping or pain (0.2%), and others (0.4%).

There were no cases of uterine tachysystole. One case of uterine hyperstimulation was identified (0.2%). No hyperstimulation was observed in the subgroup of women with a previous cesarean section (n=41). One case of non-reassuring CTG, not associated with uterine hyperstimulation, was reported during cervical ripening for a post-term pregnancy. Four percent of women experienced spontaneous rupture of membranes and 2% had spontaneous dilator expulsions. These events were considered by investigators as signs of impending labor. Infections were noted in 3.2% of patients which included chorioamnionitis, urinary tract infections, endometritis, and wound infection. However, none of these were deemed to be attributed to the effects of Dilapan-S use after clinical review by the local clinicians. Postpartum infection rate was 1.8%.

2 Synthetic osmotic dilators in the induction of labour – an international multicentre observational study

Table 2: Maternal and neonatal outcomes

Outcome	Dilapan-S (% of 444)
Uterine tachysystole	0
Uterine hyperstimulation	0.2
Spontaneous rupture of membranes	4
Spontaneous dilator expulsions	2
Bleeding during insertion/removal	2.7
Cramping or pain	0.2
Other	0.4
Maternal infections (included chorioamnionitis, urinary tract infections, endometritis, and wound infection)	3.2
Neonatal meconium	11.7
Apgar score <7 at 5 minutes in 3 newborns Cord gases with an arterial pH of <7.10 in 8 neonates 9 neonatal intensive care unit admissions	

INVESTIGATOR CONCLUSIONS: Our study is the first and the largest multicentre international cohort study evaluating the effects of Dilapan-S as a cervical ripening agent prior to induction of labour in term as well as preterm pregnancies.

This study has shown that Dilapan-S has similar qualities to mechanical dilators thus offering a safe and effective alternative for induction of labour. Further clinical trials comparing Dilapan-S to other cervical ripening agents are needed. Two randomized controlled trials were conducted in the United Kingdom and the United States to address this (clinicaltrials.gov NCT03001661 and NCT02899689).

3 Cervical ripening with an osmotic dilator (Dilapan-S) in term pregnancies – an observational study

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PUBLICATION: *Journal of Gynecology and Neonatal Biology.* 2015;1(3):1-6. doi:10.15436/2380-5595.15.015

PURPOSE: A growing number of patients are aiming to achieve vaginal birth after cesarean section (VBAC). No pharmacological agent is licensed in this group of patients. Dilapan-S is now available for cervical ripening, and is indicated also for patients with a previous cesarean section. This was a pilot study to evaluate the safety and efficacy of mechanical ripening of the cervix using Dilapan-S in a representative cohort of patients that presented in a tertiary perinatal center in Berlin, Germany with an indication for labor induction.

METHODS: This is a non-interventional, observational study of 83 patients with ≥36 gestational weeks that had previously presented at a tertiary perinatal center in Berlin, Germany and were scheduled for labor induction. The patients were pregnant with singletons, vertex presentation and had intact membranes with an unfavorable cervix (Bishop score of less than 4). Outcomes measured were: Bishop score throughout the procedure, mode of delivery, maternal and fetal outcomes, method of labor induction following cervical ripening, and indications for inducement. The application of Dilapan-S was an outpatient procedure with a pre/post CTG monitoring and then low risk (no cesarean history) patients discharged to home. Dilapan-S was left in overnight and the patient returned to the clinic the next morning. In the first round of Dilapan-S only one rod was inserted.

RESULTS: 83 patients were included that had a mean baseline Bishop score of 2 and mean gestation of 40 weeks. In total, 65% (45/83) delivered vaginally including 4.8% ventouse/forceps. The group who sought VBAC had a slightly higher vaginal delivery rate which was 75% (8/13) **(See Table 1)**. Average time from cervical ripening to delivery was 1.5 days (36 hours) with low risk patients being allowed to go home overnight (at least 12 hours). Most common indications for labor induction were prolonged pregnancy, gestational diabetes, and previous cesarean section. Multiparous women had a significantly higher chance of vaginal birth. (82.6% vs. 60.2% in total, *P*=.019).

3 Cervical ripening with an osmotic dilator (Dilapan-S) in term pregnancies – an observational study

Table 1: Mode of delivery: vaginal, forceps/ventouse (vacuum) or cesarean

Delivery history			Mode of delivery			Total
			Vaginally	Ventouse	Cesarean	
Cesarean section in previous pregnancy	No	Number	42	3	26	71
		%	59.2	4.2	36.6	100
	Yes	Number	8	1	3	12
		%	66.7	8.3	25.0	100
Total		Number	50	4	29	83
		%	60.2	4.8	34.9	100

Maternal and fetal outcomes were also assessed. One patient suffered from postoperative wound infection after cesarean section. In this instance the operation was performed due to failure to progress. There were no signs of amniotic infection syndrome and no fever at time of cervical ripening/labor induction in this case. One patient that delivered vaginally suffered from a perineal tear, grade ≥III. No other complications, such as uterine hyperstimulation and/or excessive bleeding ≥1000 mL, were found.

INVESTIGATOR CONCLUSIONS: The application of Dilapan-S is cost-effective as patients can be seen in outpatient care. The device is efficient and safe. It is an attractive option for physicians and patients to lower the cesarean section rate by facilitating VBAC.

4 Cervical ripening efficacy of synthetic osmotic cervical dilator compared with oral misoprostol at term: a randomized controlled trial

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PUBLICATION:
Obstetrics & Gynecology. 2022;139(6):1083-1091. doi:10.1097/AOG.0000000000004799

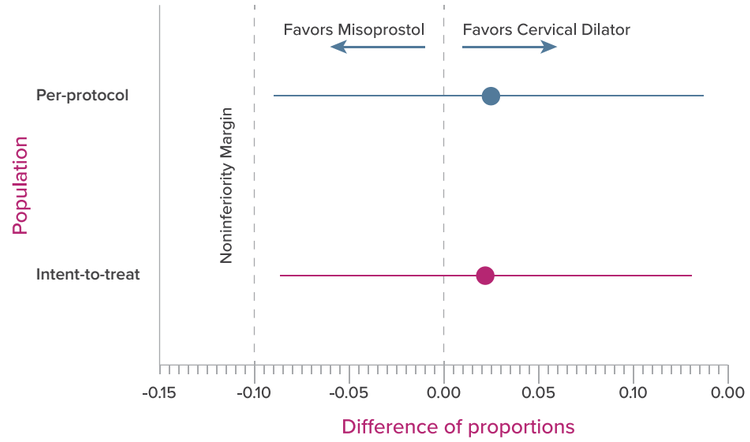
PURPOSE:
To evaluate whether a synthetic osmotic cervical dilator (Dilapan-S) is noninferior to oral misoprostol for cervical ripening as evidenced by accomplishing a vaginal delivery within 36 hours of initiation of study intervention.

METHODS:
Comparison of **M**isoprostol **R**ipening **E**fficacy with **D**ilapan (COMRED; NCT03670836) was a prospective, open label, randomized controlled noninferiority trial conducted at 2 US medical centers from 2017 to 2021. Pregnant women undergoing induction of labor at 37+ weeks' gestation with Bishop scores <6 (unfavorable cervix) were randomized to either mechanical cervical dilation or oral misoprostol. Participants in the mechanical dilation group underwent insertion of synthetic osmotic cervical dilator rods, and those in the misoprostol group received up to 6 doses of 25 micrograms orally every 2 hours. Participants in both groups remained in the labor and delivery department, but those in the Dilapan-S group were allowed to ambulate, shower and have light meals, whereas those in the misoprostol group were required to have continuous fetal heart rate monitoring. After 12 hours of ripening, oxytocin was initiated, with artificial rupture of membranes. Management of labor was at the physician's discretion. The primary outcome was the proportion of women achieving vaginal delivery within 36 hours of initiation of study intervention. Secondary outcomes included increase in Bishop score, mode of delivery, induction-to-delivery interval, total length of hospital stay, maternal and fetal safety, and patient satisfaction. According to the noninferiority hypothesis, primary analyses were conducted on both the intention-to-treat (ITT) and per-protocol populations. The ITT population included participants who were analyzed in accordance with their randomized study treatment (ie, the treatment group to which they were originally allocated, regardless of the treatment that was actually received).

4 Cervical ripening efficacy of synthetic osmotic cervical dilator compared with oral misoprostol at term: a randomized controlled trial

RESULTS:
In the study, 307 women were randomized to either Dilapan-S (n=154) or oral misoprostol (n=153). No significant differences in demographics or baseline characteristics were noted in the ITT population. The groups were well-balanced for all characteristics at baseline. Multiparous and nulliparous participants were equally distributed between the two groups with nulliparous representing 53.6% of the Dilapan-S group and 53.3% of the misoprostol group. The most common indication for induction of labor was post-term pregnancy, followed by elective induction. The proportion of women achieving vaginal delivery within 36 hours was higher with mechanical cervical dilation compared with misoprostol (61.6% vs 59.2%), with an absolute difference of 2.4% (95% CI, 29% to 13%), indicating noninferiority for the prespecified margin (**See Figure 1**). No differences were noted in the mode of delivery. Secondary outcomes (vaginal delivery rate, cesarean delivery rate, or change in Bishop score) did not differ between groups. There was no difference in mean initiation of cervical ripening-to-delivery interval in the two groups either. Total mean duration of hospitalization was similar.

Figure 1. Primary outcome: vaginal delivery within 36 hours



Absolute difference in vaginal delivery rate (with 95% CI) between cervical dilator and misoprostol in the intention-to-treat and per-protocol analysis. The 95% CI spans 0 but lies wholly above the Δ margin, indicating noninferiority.

Interventions demonstrated similar safety profiles, with uterine tachysystole during cervical ripening showing a significant difference (53.6% in the misoprostol group vs 25.7% in the Dilapan-S group, *P*<.01) (**See Table 1**). However, it should be noted that only 41.4% of patients in the misoprostol group had no complications and received all 6 scheduled doses.

4 Cervical ripening efficacy of synthetic osmotic cervical dilator compared with oral misoprostol at term: a randomized controlled trial

Table 1. Select maternal and neonatal complications in the ITT population

Complications of the method	Dilapan-S n=151, (%)	Misoprostol n=152, (%)
Uterine tachysystole[a]	35 (23.3)	70 (46.4)
	RR (95% CI): 0.50 (0.36-0.71) *P*=.01	
Uterine hyperstimulation with nonreassuring FHR tracing[b]	4 (2.6)	13 (4.3)
	RR (95% CI): 0.37 (0.12-1.12) *P*=.03	
5-min Apgar score <7	0	1 (0.7)
Cord pH <7.1	0	4 (2.6)
Uterine hyperstimulation	4 (1.6)	6 (2.0)

FHR, fetal heart rate; RR, relative risk
[a] More than five contractions per 10-minute period, averaged over 30 minutes.
[b] More than five contractions per 10-minute period, with abnormal fetal heart rate changes.

A patient satisfaction survey revealed strong agreement in several domains. Patients who received Dilapan-S reported lower pain scores (scores of ≥5 on a 1 to 10 point scale; *P*=.02), had less abdominal discomfort than with oral misoprostol (strong agreement that sensations were unpleasant, 24% vs 37%, respectively; *P*=.04), and were able to sleep more (strong agreement 65% vs 47%, respectively; *P*=.03) during cervical ripening.

INVESTIGATOR CONCLUSIONS: In summary, we present level 1 evidence that synthetic osmotic cervical dilator is an efficacious mechanical method for cervical ripening at term. Patient satisfaction was higher compared with oral misoprostol, with lower rates of tachysystole in the synthetic osmotic cervical dilator group. In addition, the safety profile of the synthetic osmotic cervical dilator makes it an optimal method for cervical ripening in the outpatient setting among low-risk women undergoing induction of labor, providing potential cost savings compared with ripening approaches requiring inpatient monitoring. We are presently completing a randomized controlled trial comparing inpatient with outpatient cervical ripening with synthetic osmotic cervical dilator in women with low-risk pregnancies.

5 A randomized trial of synthetic osmotic cervical dilator for induction of labor vs dinoprostone vaginal insert

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PUBLICATION:
American Journal of Obstetrics and Gynecology Maternal Fetal Medicine (MFM). 2022;4(4):100628. doi:10.1016/j.ajogmf.2022.100628

PURPOSE:
To compare the efficacy, maternal and neonatal safety, and maternal satisfaction of Dilapan-S with prostaglandin E_2 in the form of 10 mg-controlled release vaginal pessary, dinoprostone.

METHODS:
SOLVE was an open-label superiority randomized controlled trial in 4 English hospitals. The study included pregnant women scheduled for induction of labor with a singleton pregnancy at ≥37 weeks' gestation (determined by ultrasound dating scan), and with the fetus in a vertex presentation with intact membranes were eligible for inclusion. The need to have a preintervention Bishop score of ≤6 was also removed in April 2018 to eliminate the need for a vaginal examination solely to assess eligibility. The recruiting sites could choose whether to recruit women who had a previous cesarean delivery or myomectomy based on their local policy. These women were at an increased risk of uterine rupture with dinoprostone use. According to the protocol, up to 5 Dilapan-S dilators were inserted and left for a minimum of 12 hours and up to a maximum of 24 hours. If the cervix remained unfavorable after the first series (Bishop score <6) a second (then third) series of dilators were placed for an additional 12 to 24 hours. Dinoprostone was administered high up into the posterior vaginal fornix. Each series of dinoprostone inserts remained in place for up to 24 hours or up to 32 hours, according to local hospital policy. In both groups, if spontaneous labor had not started, amniotomy was conducted after the Bishop score was ≥6. Oxytocin infusion using a syringe pump was used as per hospital protocols, commencing no sooner than 30 minutes after the removal of the last series of Dilapan-S or dinoprostone and with continuous fetal monitoring. The primary outcome was failure to achieve vaginal delivery (ie, cesarean delivery). Secondary outcome measures included maternal outcomes (time to vaginal delivery after randomization, use of analgesia, change in Bishop score, etc.), maternal and neonatal adverse events, and maternal satisfaction. Maternal satisfaction was assessed using a patient satisfaction questionnaire.

5 A randomized trial of synthetic osmotic cervical dilator for induction of labor vs dinoprostone vaginal insert

RESULTS:
In the study, 674 women were randomized to either Dilapan-S (n=337) or prostaglandin E_2 vaginal insert (dinoprostone [n=337]). *The trial did not reach its planned sample size of 860 due to restrictions on research during the COVID-19 pandemic.*

The groups were well-balanced for all characteristics at baseline. In the overall study, most patients were nulliparous (n=541, 80.3%) and nearly 20% were multiparous (n=133, 19.7%). In the Dilapan-S group, 79.8% of patients were nulliparous and 80.7% were nulliparous in the dinoprostone group. The most common indications for induction of labor were post-term pregnancy, intrauterine growth restriction and/or oligohydramnios, and reduced fetal movements. The total duration of cervical ripening was comparable across groups. First round cervical ripening success rate (defined as not requiring a second series of rod or pessary insertion) was greater in the in the Dilapan-S group (78.9%) vs the dinoprostone group (69.0%). Slow progress or failure to ripen was reported as a reason for unsuccessful first rounds in 55 women in the Dilapan-S group compared to 71 women in the dinoprostone group. The intervention fell out in 0 women in the Dilapan-S group compared to 13 women in dinoprostone group.

Failure to achieve vaginal delivery (ie, cesarean delivery) rate was 37.4% in the Dilapan-S group vs 34.3% in the dinoprostone group (**See Table 1**). Use of analgesia during cervical ripening was significantly more frequent in the dinoprostone group compared to the Dilapan-S group (**See Table 1**); this included oral opioid use (dinoprostone 43.9% vs 21.4% Dilapan-S, respectively) and pethidine (meperidine) use (17.5% vs 6.2%, respectively). Mean time between removal of last series of interventions to amniotomy was similar for both groups, but significant differences in amniotomy undertaken for induction of labor and oxytocin required for induction of labor were also observed between groups (**See Table 1)**.

5 A randomized trial of synthetic osmotic cervical dilator for induction of labor vs dinoprostone vaginal insert

Table 1. Maternal outcomes

Outcome	Dilapan-S n=337 (%)	Dinoprostone n=337 (%)	Adjusted RR/GMR (95% CI), *P* value
Failure to achieve vaginal delivery (cesarean delivery)	126 (37.4)	115 (34.3)	RR[a] 1.10 (0.90-1.35), *P*=.33
Use of analgesia during cervical ripening	170 (51.2)	220 (66.3)	RR[a] 0.77 (0.67-0.87), *P*<.0001
Time between randomization and start of analgesia use for cervical ripening (hr)	Geometric mean		GMR[b] 0.49 (0.38-0.62), *P*<.0001
	5.3	10.8	
Any complications during cervical ripening	35 (10.5)	66 (20.2)	RR[c] 0.52 (0.35-0.79) *P*=.0021
Time between removal of last series of intervention to amniotomy (hr)	Geometric mean		GMR[b] 1.08 (0.78-1.49) *P*=.63
	12.7	14.5	
Amniotomy undertaken for induction of labor	235 (70.2)	141 (42.6)	RR[a] 1.64 (1.43-1.89) *P*<.0001
Time between first insertion of intervention to when labor started (hr)	Geometric mean		GMR[b] 1.34 (1.19-1.52), *P*<.0001
	45.9	35.0	
Required oxytocin for induction of labor	120 (62.7)	130 (39.3)	RR[d] 1.60 (1.28-1.99) *P*<.0001
Length of stay from randomization (d)	Median (IQR)		n/a
	4 (3.0-6.0)	4 (3.0-6.0)	

CI, confidence interval; GMR, geometric mean ratio; IQR, interquartile range; RR, risk ratio
[a] Risk ratio is estimated using a binomial model with a log link adjusting for age, BMI, and parity as fixed effects; [b] The geometric mean ratio is estimated using a mixed effect linear regression adjusted for minimization variables and randomizing center as a random effect; [c] Risk ratio is estimated using a mixed Poisson model, with a log link adjusting for age, BMI, and parity as fixed effects and randomizing center as a random effect; [d] The risk ratio is estimated using a mixed binomial model with a log link adjusting for age, BMI, and parity and randomizing center as a random effect.

There were more occurrences when dinoprostone was removed because of complications; 68 compared with 19 women in the Dilapan-S group, principally owing to uterine tachysystole (11 events vs 1 event, respectively), uterine hyperstimulation with a nonreassuring fetal heart rate (13 vs 0 participants, respectively), and abnormal cardiotocograph changes (34 vs 6 fetuses, respectively) (**See Table 2**). There is no evidence of any differences in neonatal outcomes between the groups.

5 A randomized trial of synthetic osmotic cervical dilator for induction of labor vs dinoprostone vaginal insert

Table 2. Complications in the as treated population

Outcome	Dilapan-S n=251 (%)	Dinoprostone n=302 (%)
During cervical ripening	19 (7.6)	68 (22.6)
Uterine tachysystole	170 (51.2)	220 (66.3)
Uterine hyperstimulation with nonreassuring or abnormal FHR	0 (—)	220 (66.3)
Effect on fetus (CTG [cardiotocograph])	6 (2.4)	34 (11.3)
During or after labor	184 (73.3)	223 (73.8)
Uterine hyperstimulation	4 (1.6)	6 (2.0)

There were substantially better outcomes regarding maternal satisfaction during cervical ripening period with Dilapan-S compared to dinoprostone (**See Table 3**).

Table 3. Select results from a maternal satisfaction survey*

	Dilapan-S	Dinoprostone
Get some sleeping time	48.0%	22.1%
Get some time to relax	52.9%	27.9%
Perform daily activities	76%	46.9%
Did not feel any discomfort with drug or device in place	46.2%	22.7%
Less pain with drug or device in place	mean 3.1[a]	mean 5.6[a]
Lower use of analgesia during cervical ripening	51.2%	66.3%
	P<.0001	
Lower use of oral opioids	21.4%	43.9%

[a] Scale of response ranges from 0–10; higher scores indicate a more negative response.

* Not all patients enrolled in the trial returned their satisfaction questionnaire (questionnaires received: Dilapan-S group, 260 of 337; dinoprostone group, 231 of 337).

5 A randomized trial of synthetic osmotic cervical dilator for induction of labor vs dinoprostone vaginal insert

INVESTIGATOR CONCLUSIONS: Evidence from this study has shown that women undergoing induction of labor with Dilapan-S have similar rates of cesarean delivery and maternal and neonatal adverse events compared with dinoprostone. This suggests that a slower approach to cervical ripening with Dilapan-S as opposed to the more rapid onset of ripening achieved by prostaglandins can be offered to women, following a discussion of the relative benefits of each approach.

MEDICEM CONCLUSIONS: Intrauterine growth restriction and reduced fetal movements represent a group of women with reduced fetal reserve where Dilapan-S would be a benefit as it is associated with a lower risk of uterine hyperstimulation. This would suggest that Dilapan-S could also be used for cervical ripening as an outpatient procedure.

Because of the timing of this study, and due to demands on the clinical service, not all women were able to receive a timely amniotomy once a favorable cervix had been achieved, potentially pausing or reversing the physiological process of cervical ripening. Therefore, the occurrence of cesarean delivery should be viewed in relation to the high proportion of nulliparous participants and delayed amniotomies due to demands on the clinical service during the COVID-19 pandemic.

6 A prospective pilot study of Dilapan-S compared with Propess for induction of labour at 41+ weeks in nulliparous pregnancy

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PURPOSE:
The incidence of labor induction has risen worldwide over the past decade, and this may contribute to the rising cesarean delivery rate. The mechanisms for induction of labor are generally divided into two categories: mechanical and pharmacological. The objective of this pilot study was to determine if mechanical induction with Dilapan-S was an acceptable and safe method of induction of labor (IOL) compared with pharmacological induction with dinoprostone 10 mg (Propess) in post-dates uncomplicated nulliparous women.

METHODS:
This was a prospective comparative pilot study of nulliparous women scheduled for induction of labor for post-dates (≥41 weeks' gestation) with an unfavorable cervix (Bishop score ≤6) conducted at the National Maternity Hospital in Dublin. Patients were treated with 1-5 rods of Dilapan-S for up to 24 hours versus routine induction of labor with Propess for up to 24 hours. If the cervix was still unfavorable at reassessment after Dilapan-S or Propess use, up to two prostin (intracervical PGE_2) gels were used. The primary outcome measures of this study were study protocol compliance and maternal and fetal safety outcomes including infection, uterine hyperstimulation, and neonate Apgar scores. The secondary outcome measures of this study included Bishop score changes, duration of ripening agent in situ, duration of induction to delivery, mode of delivery within 24 hours, additional use of prostaglandin and/or oxytocin for labor induction, and neonatal complications.

RESULTS:
Women were recruited from May until November 2016 with 25 receiving Dilapan-S and 26 receiving routine care (Propess). Compliance to study protocol was 25/26 (96%). There were no differences in maternal and neonatal primary outcomes between the groups **(See Table 1)**. There were no cases of hyperstimulation with either group. There were no differences in secondary outcomes including infection, cesarean delivery rate, the mean change in Bishop score, and neonatal complications **(See Table 2)**.

6 A prospective pilot study of Dilapan-S compared with Propess for induction of labour at 41+ weeks in nulliparous pregnancy

Table 1: Primary efficacy and safety outcomes

	Dilapan-S n=26 (%)	Propess n=26 (%)	Statistical *P* value
Hyperstimulation	0 (0)	0 (0)	1.00
Maternal infection	4 (15.4)	4 (15.4)	1.00
Neonatal infection	4 (15.4)	4 (15.4)	1.00
Apgar <7 at 1 minute	1 (3.8)	0 (0)	1.00
Apgar <9 at 5 minutes	1 (3.8)	1 (3.8)	1.00

Table 2: Secondary efficacy and safety outcomes

	Dilapan-S n=26	Propess n=26	Statistical *P* value
Change in Bishop score	3.3 (mean SD 2.4)	3.7 (mean SD 2.5)	.559
Complications*	1 (3.8%)	1 (3.8%)	1.00
Median time of induction agent in situ (hours)	22.8 (mean SD 7.7)	17.3 (mean SD 5.6)	.005
Median time to delivery (hours)	39.5 (mean SD 14.6)	34.6 (mean SD 13.9)	.221
Delivery within 24 hours	5 (19.2%)	4 (15.4%)	1.00
Cesarean delivery	7 (26.9%)	14 (53.8%)	.089
Instrumental delivery	10 (38.4%)	7 (26.9%)	.555
Additional use of prostaglandin 1st	10 (38.4%)	4 (15.4%)	.116
Additional use of prostaglandin 2nd	1 (3.8%)	0 (0%)	1.00
Use of oxytocin	17 (65.4%)	17 (65.4%)	1.00
Epidural in labor	22 (84.6%)	22 (84.6%)	1.00
Third- and fourth-degree tears	0 (0%)	0 (0%)	1.00
MROP (manual removal of placenta)	1 (3.8%)	0 (0%)	1.00
PPH (postpartum hemorrhage) >1 L	2 (7.7%)	0 (0%)	.490
Blood transfusion	1 (3.8%)	0 (0%)	1.00
NICU admission	0 (0%)	0 (0%)	1.00
Meconium at delivery	3 (11.5%)	3 (11.5%)	1.00

*Dilapan-S: 1 spontaneous expulsion; Propess: 1 spontaneous expulsion.

6 A prospective pilot study of Dilapan-S compared with Propess for induction of labour at 41+ weeks in nulliparous pregnancy

INVESTIGATOR CONCLUSIONS: Dilapan-S is an acceptable, safe form of induction of labor in post-dates uncomplicated nulliparous pregnancy. No cases of hyperstimulation were found, and therefore, Dilapan-S may be a suitable option for outpatient induction of labor in low risk post-dates nulliparous pregnancy.

7 Pilot study. Mechanical versus pharmacological term induction: a cohort group analysis of maternal and neonatal outcome: hygroscopic cervical dilator versus prostaglandin E_2

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Clinical Obstetrics, Gynecology and Reproductive Medicine, 2016;2(4):217-220. doi:10.15761/COGRM.1000154

PURPOSE:
The objective of this study was to compare induction time and maternal as well as fetal outcomes between Dilapan-S (a hygroscopic cervical dilator) and two prostaglandin E_2 application methods during term induction of labor.

METHODS:
The study enrolled pregnant women with a singleton fetus in vertex presentation, at or above 36+1 weeks' gestation, and no cesarean history from January to May 2015 for Dilapan-S and March 2013 to August 2013 for PGE_2. The Dilapan-S group had a max of 5 rods inserted. The inserted rods were removed when the patient was in active labor or on the next day (<24 hours). After removing the rods and if the patient was not in active labor all patients received intravaginal PGE_2 1 mg (Minprostin®). The intracervical PGE_2 group had a cannula inserted in the cervix and application of the 0.5 mg PGE_2 gel (Prepidil®). In the absence of regular contraction, another 0.5 mg gel was applied into the cervix. The intravaginal PGE_2 group first received 1 mg Minprostin and in the absence of regular contraction another 2 mg was applied after 6 to 8 hours. On the 2nd day of induction, initially 2 mg and after 6 to 8 hours another 1 mg were applied if no regular contraction was felt by the patient. CTG was done for 30 minutes pre/post Dilapan-S and 30 minutes before PGE_2 applications and post for 60 minutes. Outcomes measured were induction-to-delivery interval (from insertion of first rods or gel to birth), number of fetal blood samples, PDA rate, rate of oxytocin augmentation, 5-minute and 10-minute Apgar score, and arterial pH value.

7 Pilot study. Mechanical versus pharmacological term induction: a cohort group analysis of maternal and neonatal outcome: hygroscopic cervical dilator versus prostaglandin E_2

RESULTS:
A total of 63 patients were enrolled in this study with 24 in the Dilapan-S group, 20 in the PGE_2 intracervical gel group and 19 in the PGE_2 intravaginal gel group. Median induction time to delivery was statistically significantly shorter in the intracervical (12.8 hours) compared to Dilapan-S (31.7 hours) or the intravaginal (12.8 hours) group. No difference in induction-to-delivery time was found between Dilapan-S and intravaginal PGE_2 (*P*>.05). With intracervical PGE_2 high levels of uterine hyperstimulation (25%) were detected which all required pharmacological intervention with fenoterol. Intravaginal PGE_2 only rarely (5%) caused uterine hyperstimulation, whereas Dilapan-S showed no hyperstimulation at all. No significant difference was seen between neonatal 5-minute and 10-minute Apgar scores, and arterial pH value. Four patients with premature rupture of membranes were included in the Dilapan-S study group. There were no neonatal or maternal infections.

INVESTIGATOR CONCLUSIONS: The intracervical PGE_2 had the shortest induction-to-delivery time in comparison to intravaginal PGE_2, and mechanical induction with Dilapan-S. With intracervical PGE_2 high levels of uterine hyperstimulation (25%) were detected which all required pharmacological intervention with fenoterol. Intravaginal PGE_2 only rarely caused uterine hyperstimulation, whereas there was no hyperstimulation with Dilapan-S.

8 Outpatient compared with inpatient preinduction cervical ripening using a synthetic osmotic dilator: a randomized clinical trial

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PUBLICATION:
Saad AF, Gavara R, Senguttuvan RN, et al. Outpatient compared with inpatient preinduction cervical ripening using a synthetic osmotic dilator: a randomized clinical trial. *Obstet Gynecol.* 2022;140(4):584-590. doi:10.1097/AOG.0000000000004942

PURPOSE:
To assess whether outpatient cervical ripening with a synthetic osmotic dilator (Dilapan-S) shortens the length of hospital stay in term pregnancies undergoing labor induction. Various ripening methods are available; mechanical methods of cervical ripening are safe and cost-effective. Rates of labor induction in 2019 rose to 29.4%, with a third of patients requiring cervical ripening. Bolstered by recent evidence on the use of mechanical dilators and their limited effect on uterine contractility, there is support for allowing participants to go home after insertion. Dilapan-S, an FDA approved device for cervical ripening was noninferior to the Foley balloon and oral misoprostol in terms of safety and efficacy with better patient satisfaction. Allowing pregnant women to return home after insertion is a promising strategy that lowers in-hospital healthcare costs and improves subject satisfaction.

METHODS:
HOMECARE was a multicenter prospective randomized controlled trial that enrolled 339 pregnant women scheduled for induction of labor at term with an unfavorable cervix (<3 cm dilated and <60% effaced) and without a need for maternal or fetal continuous monitoring from 2 academic centers in the United States. Patients were randomized to the outpatient (n=167) or inpatient arm (n=171); 1 patient withdrew from the study. Women in the outpatient arm were asked to return after 12 hours or earlier if needed. Women in the inpatient arm remained in the hospital. The primary outcome was the proportion of women with hospital stay >48 hours. Secondary outcomes included vaginal delivery within 24, 36, and 48 hours, change in cervical dilation, change in Bishop score, analgesics used during cervical ripening, removal of Dilapan-S <12 hours, hospital stay, time from admission to active stage of labor (defined as ≥6 cm cervical dilation), time from device placement to active phase, time from device placement to delivery, composite and individual adverse neonatal outcomes and maternal outcomes. Each patient was also asked to complete a satisfaction survey regarding sleep, rest, pain, and activity.

8 Outpatient compared with inpatient preinduction cervical ripening using a synthetic osmotic dilator: a randomized clinical trial

RESULTS:
Baseline characteristics did not differ among groups. The mean number of Dilapan-S rods inserted was 5 in both groups. The proportion of women with hospital stay >48 hours was significantly lower in the outpatient group (**See Figure 1**). The outpatient group had a shorter total length of hospital stay and shorter time from admission to active labor. Four out of 167 outpatient subjects were admitted <12 hours for suspected labor and rupture of membrane. Delivery within 24 hours of admission was statistically significantly higher in the outpatient group (70.1%) than the inpatient group (50.3%) (RR 1.39 [CI: 1.16-1.67], *P*<.001). Analgesic use during cervical ripening was also significantly lower in the outpatient group (3.6%) vs the inpatient group (15.8%) (RR 0.23 [CI: 0.1-0.54], *P*<.001). Route of delivery and other maternal and neonatal outcomes were not significantly different between groups. Total length of hospital stay (in hours) and time from admission to active stage of labor, which was defined as dilation >5 cm, were also significantly lower in the outpatient group (**See Figure 2A, 2B**). The patient satisfaction survey revealed that women were significantly more able to walk, eat, and shower in the outpatient group and felt that outpatient cervical ripening was beneficial and would choose the same approach for their subsequent pregnancy.

Figure 1: Hospital stay >48 hours.

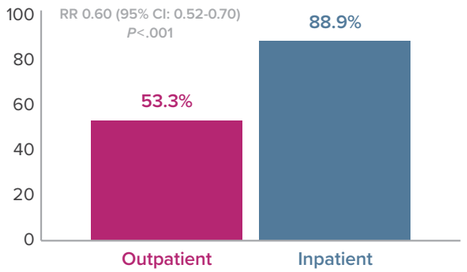
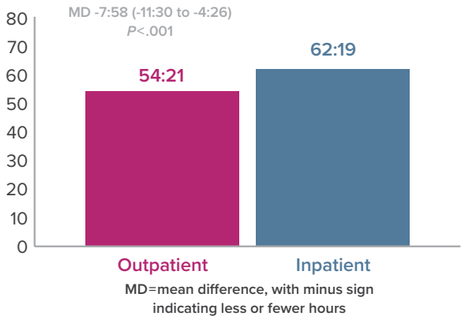
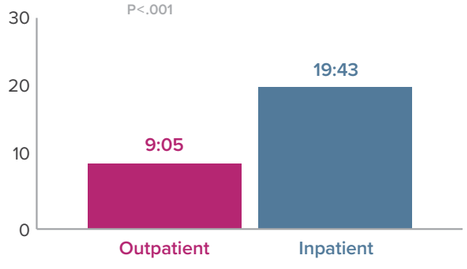


Figure 2A: Total length of hospital stay in hours:minutes (hr:min).



MD=mean difference, with minus sign indicating less or fewer hours

Figure 2B: Time from admission to active stage of labor (defined as dilation >5 cm)—median in hours:minutes (hr:min).



MD=mean difference; RR=relative risk

8 Outpatient compared with inpatient preinduction cervical ripening using a synthetic osmotic dilator: a randomized clinical trial

INVESTIGATOR CONCLUSIONS: Outpatient cervical ripening with Dilapan-S reduced (or decreased) hospital stay for more than 48 hours without increasing adverse events. Eighty-five percent of patients did not require a second round of cervical ripening, and participants in the outpatient group used analgesia less frequently than those in the inpatient group. The trial was not powered to detect statistically significant differences in maternal infection, chorioamnionitis, cesarean delivery rates, and neonatal outcomes. Outpatient cervical ripening with a synthetic osmotic dilator that reduced hospital stay compared with inpatient ripening with better patient satisfaction and pain control. Future studies and analyses are needed to assess cost benefits, neonatal safety, maternal infection, and mode of delivery.

MEDICEM CONCLUSION: The evidence supports the benefit and safety of outpatient mechanical cervical ripening.

9 Induction of labor in patients with an unfavorable cervix after a cesarean using an osmotic dilator versus vaginal prostaglandin

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PURPOSE:
There is insufficient information from randomized controlled trials on which to base clinical decisions regarding the optimal method of induction of labor in women with a prior cesarean delivery (CD) and an unfavorable cervix. In general, induction of labor using mechanical methods results in similar cesarean rates as prostaglandins but at a lower risk of uterine hyperstimulation. Therefore, the objective of this pilot study was to compare the application of an osmotic dilator (Dilapan-S) to vaginal prostaglandin gel (Minprostin®) to exclude major safety issues.

METHODS:
This pilot study gathered data from 82 women attempting TOLAC (at least 1 cesarean history) between 2011 and August 2016 at a public tertiary care clinic. This study analyzes and retrospectively compares two groups: cervical ripening with Dilapan-S or dinoprostone (Minprostin). All patients had a baseline Bishop score of <6. Up to five rods were inserted during one session and left in the cervical canal for 12 hours to a maximum of 24 hours. A 45-minute pre/post CTG monitoring was performed, and all patients were admitted to the hospital.

RESULTS:
Data was collected from 82 women with a previous CD and median gestational week of 41. Results concerning the delivery mode were not statistically different between groups. The vaginal delivery rate including forceps/ventouse (vacuum) was the same (55%) after cervical ripening with Dilapan-S (n=33) and dinoprostone vaginal gel (n=49). The time period from application of the cervical ripening agent to onset of labor was longer with Dilapan-S versus dinoprostone (mean of 36 hours and 17.1 hours respectively), but the time from onset of labor to delivery was similar (mean of 4.4 hours and 4.9 hours respectively). More patients in the Dilapan-S group versus dinoprostone group received oxytocin and/or had amniotomy performed **(See Table 1)**.

9 Induction of labor in patients with an unfavorable cervix after a cesarean using an osmotic dilator versus vaginal prostaglandin

Table 1: Obstetric outcome: Mode of delivery, time from admission to the hospital to delivery, with different time points (Welch's two sample t-test); induction of labor with oxytocin and amniotomy (Fisher's exact test for count data).

Characteristic	Dilapan-S (n=33)	dinoprostone (n=49)	Statistical test and *P* value
Vaginal birth	15 (45%)	22 (45%)	Fisher's exact test for count data *P*=.8649
Ventouse	3 (10%)	3 (6%)	—
Secondary cesarean delivery	15 (45%)	24 (49%)	—
Time from admission to the hospital to delivery (hours, mean ± SD)			
Dilapan-S insertion/dinoprostone application to onset of labor	36 ± 19.7	17.1 ± 14.2	<.001
Onset of labor with oxytocin and amniotomy	4.4 ± 8.2	4.9 ± 4.6	.7474
Induction of labor with oxytocin and amniotomy			
Oxytocin application	32 (97%)	25 (51%)	.2584
Amniotomy	21 (64%)	24 (49%)	—

Maternal and fetal outcomes were also assessed. Less uterine hyperstimulation and/or pathological CTG pattern was observed in the group using Dilapan-S. In the Dilapan-S group 1 patient had a uterine scar dehiscence and another woman was treated for postoperative peritonitis after CD. In the dinoprostone group, 1 patient had a uterine rupture with an overall blood loss of 10 liters, another had a uterine scar dehiscence. Due to the small size of the cohort, these numbers are not representative. No significant differences were found between groups in Apgar score and average umbilical artery pH. Between 97% and 92% (32/33 and 45/49) (100%, 100%) of neonates had an Apgar score of >8 after 1 minute (5, 10 minutes, respectively).

INVESTIGATOR CONCLUSIONS: This pilot study examines the application of an osmotic dilator for cervical ripening to promote vaginal delivery in women who previously delivered via cesarean section. In our experience, the osmotic dilator gives obstetricians a chance to perform induction of labor in these women.

2 2018 Gupta et al. **Synthetic osmotic dilators in the induction of labour—an international multicentre observational study.** An international, multicenter, observational study with 444 women was conducted at 11 sites in 7 countries including the United States. **41 of 444 observed patients had previous cesarean history.** PAGE 7

3 2015 Maier et al. **Cervical ripening with an osmotic dilator (Dilapan-S®) in term pregnancies–an observational study.** A pilot, observational, non-interventional study with **83 women conducted at a single center in Germany. 12 of observed patients had previous cesarean history.** PAGE 10

13 2014 Vlk et al. **Efficacy and safety of the osmotic dilator Dilapan-S® for cervical ripening in women with/without Caesarean section.** This is an observational, prospective, multicenter study in the Czech Republic, with data collection of 96 females after 36 weeks' gestation **(35 with cesarean section history)** to assess the success of cervical ripening (Bishop score), safety data, and patient satisfaction. PAGE 38

10 Experimental comparison of properties of natural and synthetic osmotic dilators

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Archives of Obstetrics and Gynecology. 2015;292(2):349-354. doi:10.1007/s00404-015-3623-3

PURPOSE:
This publication aims at supporting and explaining some of the clinically observed differences in dilation performance between synthetic dilators (Dilapan-S/Dilasoft) and laminaria with experimental laboratory data that would allow quantifying, evaluating and comparing in vitro properties of the dilators.

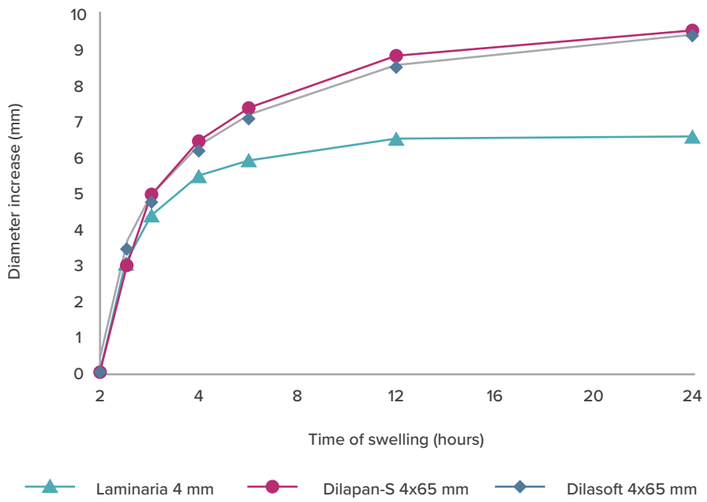
METHODS:
All experiments were carried out with Dilapan-S (3x55 and 4x65 mm), Dilasoft (3x55 and 4x65 mm), and laminaria (3 and 4 mm). Isotonic solution (0.9% w/w sodium chloride aqueous solution in demineralized water) was used as the swelling medium. Diameters were measured for 50 samples of each type of dilator, always at 3 spots of the rods (at both ends and in the middle). Measurements were carried out first in dry state. Then the dilators were placed into isotonic solution at 37°C and their diameters were measured after 1, 2, 4, 6, 12, and 24 hours. Arithmetic mean and standard deviation were calculated for each sample and subsequently each set of samples.

RESULTS:
The maximum diameter increase of 3 and 4-mm Dilapan-S was 3.6 and 3.3 times, and of Dilasoft 3.2 and 3.1 times, respectively. For laminaria, it was 2.9 and 2.7 times. The difference between synthetic dilators and laminaria was statistically significant (P=.01). Dilapan-S/Dilasoft synthetic dilators swell faster than laminaria. In 4 mm dilators, the same swelling was achieved by synthetic dilators after 4 hours and laminaria after 12 hours, while laminaria never achieved the 6-hour diameter of synthetic dilators. The average swelling speed during the first 6 hours of swelling was 1.2 mm/hour for Dilapan-S and Dilasoft and 1.0 mm/hour for laminaria **(See Figure 1)**. Under applied counter force, synthetic dilators increased their diameter more than laminaria (+3.6 mm for Dilapan-S, +3.8 mm for Dilasoft, +1.2 mm for laminaria; P=.01) and achieved faster expansion. Synthetic dilators also showed significantly higher consistency between samples in all experiments than laminaria.

Note: Dilasoft is not cleared for use in the United States.

10 Experimental comparison of properties of natural and synthetic osmotic dilators

Figure 1: Average diameter increase of 4-mm dilators as a function of time during free swelling in isotonic solution at 37 °C.



INVESTIGATOR CONCLUSIONS: Synthetic dilators compared to laminaria reached higher maximum diameters, acted faster, were more consistent and were able to expand against force three times more. The results support clinical observations that synthetic dilators are more suitable and preferable for same-day dilation and evacuation procedure and that fewer synthetic dilators are needed to achieve the same effect.

11 Predictors of vaginal delivery after cervical ripening using a synthetic osmotic dilator

AUTHORS:
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PUBLICATION:
European Journal of Obstetrics and Gynecology Reproductive Biology. 2020;246:160-164. https://www.ejog.org/article/S0301-2115(20)30057-9/fulltext.

PURPOSE:
This was a secondary analysis of a 2-year prospective multicenter international post marketing observational study of a synthetic osmotic dilator (Dilapan-S) for cervical ripening prior to induction of labor in third trimester pregnancies. Objective was to evaluate the determinants of vaginal delivery and safety in women undergoing cervical ripening with a synthetic osmotic dilator (Dilapan-S) prior to induction of labor.

METHODS:
This study involved 10 medical centers from Europe, Asia, and the US and included women ≥37 weeks of gestation, with the ability to give informed consent, who required preinduction cervical ripening or induction of labor with no contraindication to vaginal delivery. The primary outcome was to evaluate the association between Bishop score and vaginal delivery. Secondary outcomes included rate of vaginal delivery, change in Bishop scores from pre- to post-cervical dilatation, and safety outcomes, including rates of adverse events associated with the use of the dilator, like uterine tachysystole, non-reassuring fetal heart rate, vaginal bleeding, infection complications, and neonatal outcomes. Placement of Dilapan-S was at the physician's or provider's discretion.

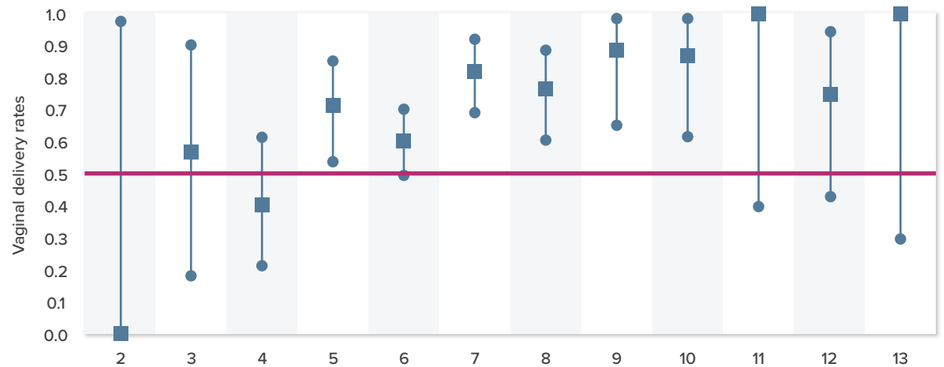
Patients were excluded if maternal age was < 18 years, informed consent could not be obtained, they were participating in other clinical trials, or induction of labor was initiated within 24 hours of their receiving the information leaflet. Association between Bishop score and vaginal delivery was evaluated with a multivariate receiver-operating characteristic (ROC) curve analysis. A Wilcoxon rank test and multivariate logistic regression were used for statistical analysis (significance: $P<.05$).

11 Predictors of vaginal delivery after cervical ripening using a synthetic osmotic dilator

RESULTS:
Between May 2015 and July 2016, 444 pregnant women were included. The most common indications for induction included late term pregnancies (37%), maternal hypertension (15%), elective induction (12%), oligohydramnios or intrauterine growth restriction (IUGR) (11%), and maternal diabetes (11%). Seventy percent of patients delivered vaginally (n=310). Compared to patients who underwent cesarean delivery, those who delivered vaginally were more likely to have a history of prior vaginal delivery. Vaginal delivery rates were significantly correlated with Bishop scores of pre and post Dilapan-S and difference. After adjusting for age, BMI, number of dilators, cervical ripening time, and gestational age, both prior vaginal delivery and post-Dilapan-S Bishop scores were strong predictors of vaginal delivery (estimate coefficient: 0.1275 ± 0.03, *P*=.0002; 0.049 ± 0.01, *P*=.0001; respectively). Aggregate ROC accounting for these variables further supported these findings (AUC=0.734). The lower confidence interval limit of vaginal delivery rates was above 50% when post-Dilapan-S Bishop scores were ≥5 **(See Figure 1)**. Cox regression analyses demonstrated that the duration of labor was significantly shorter in women that had vaginal delivery. During cervical ripening, the most common complication was bleeding at insertion or extraction (2.3%), followed by tachysystole (0.2%) and non-reassuring fetal heart rate tracing (0.2%). No additional procedures were needed to stop bleeding. No cases of dilator entrapment or fragmentation were reported throughout the cohort.

11 Predictors of vaginal delivery after cervical ripening using a synthetic osmotic dilator

Figure 1: Vaginal delivery rates and post-cervical ripening Bishop score. (confidence intervals [CI] are illustrated as circles. The lower CI limit of vaginal delivery rates was above 50% (pink line) when post-Dilapan-S Bishop scores were ≥5)



Vaginal delivery rates and post-cervical ripening Bishop scores. Confidence intervals (CI) are illustrated as circles. The lower CI limit of vaginal delivery rates was above 50% (pink line) when post-Dilapan-S Bishop scores were ≥5. (For interpretation of the references to color in this figure, the reader is referred to https://www.ejog.org/article/S0301-2115(20)30057-9/fulltext).

INVESTIGATOR CONCLUSIONS: Bishop scores after cervical ripening with Dilapan-S are good predictors of vaginal delivery. Bishop scores <5 post Dilapan-S may warrant further cervical ripening. Further level 1 trials are needed to compare osmotic dilators to other ripening methods.

12 Longitudinal ultrasound evaluation of Dilapan-S diameter during cervical ripening

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CONGRESS:
Poster presented at the Society for Maternal Fetal Medicine 42nd Annual Pregnancy Meeting, January 31-February 5, 2022.

PURPOSE:
To evaluate the diameter rate-change of each Dilapan-S rod during cervical ripening using transvaginal ultrasound. Investigators also evaluated the effects of soaked gauze placement on the rate of Dilapan-S diameter change over time.

METHODS:
This was a prospective longitudinal study of term women undergoing labor induction with a Bishop score <6. Women were randomized into two groups (soaked gauze or no gauze) stratified by parity. Using transvaginal ultrasound, maximal Dilapan-S diameters were obtained in a longitudinal plane **(See Figure 1)**. Measurements were taken at 4 pre-specified time points (3, 6, 8, and 12 hours). All Dilapan-S were removed at 12 hours after insertion. Ultrasound measurements at hour 12 were used to denote maximal rod dilations. Primary outcome was the rate of change in Dilapan-S diameter over time. Secondary analysis included rate of change according to the use of soaked gauze.

RESULTS:
The study recruited 44 women with a total of 178 Dilapan-S rods placed (an average of 4 per patient). The soaked gauze group included 22 women and there were also 22 women in the no gauze group. Mean Dilapan-S diameters (mm) were statistically significant for each time (3 hour: 7.9 mm [SD 0.09]; 6 hour: 9.4 mm [SD 0.09]; 8 hour: 10.0 mm [SD 0.09]; 12 hour: 10.9 mm [SD 0.08]; *P* value<.001). After stratifying by gauze use, there was no difference in Dilapan-S diameters at 3, 6, 8, and 12 hours respectively (*P*=0.41, 0.80, 0.35, and 0.28). Inter-observer correlation (ICC) was 0.957 (95% CI, 0.923-0.976), suggesting excellent reproducibility between sonographers. When compared to hour 12, Dilapan-S diameter reached 72%, 86%, and 92% of dilation at 3, 6, and 8 hours respectively **(See Figure 2)**.

12 Longitudinal ultrasound evaluation of Dilapan-S diameter during cervical ripening

Figure 1: Transvaginal ultrasound image of Dilapan-S at 6 hours after placement

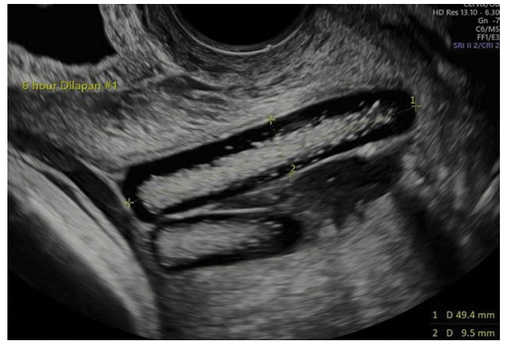
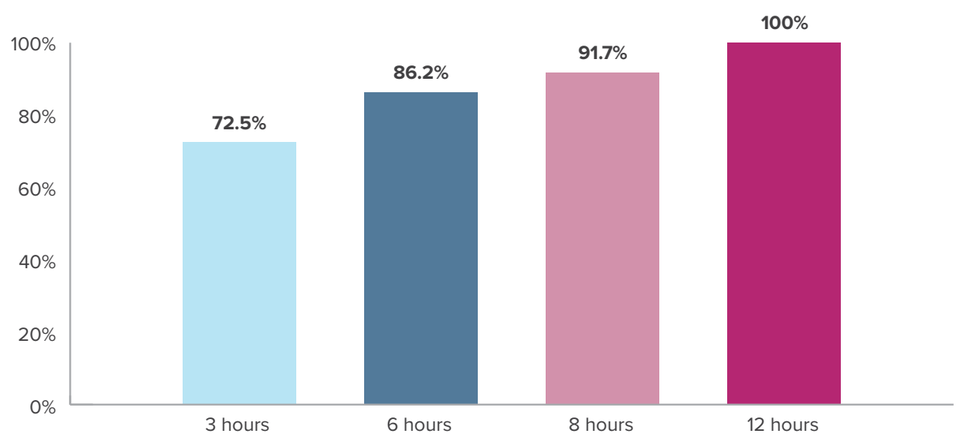


Figure 2. Percentage of Dilapan-S dilation at different time points after placement



INVESTIGATOR CONCLUSIONS: By hour 8, Dilapan-S reaches 92% of dilation compared to hour 12. Our findings are useful in planning randomized studies on shorter cervical ripening durations using Dilapan-S for labor induction.

13 Efficacy and safety of the osmotic dilator Dilapan-S® for cervical ripening in women with/without Caesarean section

AUTHORS:
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CONGRESS:
Poster presented at the 13th World Congress in Fetal Medicine, The Fetal Medicine Foundation. June 29–July 3, 2014. Nice, France.

PURPOSE:
The objective of this study was to evaluate efficacy and safety of the synthetic osmotic dilator Dilapan-S for cervical ripening prior to labor induction according to defined criteria and to compare results in females with/without cesarean section in their medical history.

METHODS:
This study was an observational, prospective, multicenter, data collection on the use of Dilapan-S performed between May 2013 and October 2013. Ninety-six women at 36+ weeks' gestation with Bishop score <4 were included in the data analysis. Nearly 37% (35/96) had a cesarean section reported in their medical history, while the group of females without previous cesarean section involved 61 women (63.5%). Assessment of the primary objective and success of cervical ripening procedure was based on the Bishop (cervical) score. Safety data collection was focused on fetal hypoxia, uterine hypertonus, clinical signs of infection and other potential adverse effects related to the use of Dilapan-S. Answers about satisfaction from patient's questionnaire were also analyzed.

RESULTS:
Dilapan-S was effective regarding Bishop score progression with a statistically significant increase from a mean of 2.81 cm to 6.13. A successful preinduction (Bishop score 5 or greater) was achieved in 86.5% of women. 71.6% (68/93) delivered vaginally, 28.4% (27/93) delivered by cesarean section. 64.7% (22/92) were successful VBACs **(See Table 1)**.

13 Efficacy and safety of the osmotic dilator Dilapan-S® for cervical ripening in women with/without Caesarean section

Table 1: Comparison of delivery mode in women with/without cesarean section

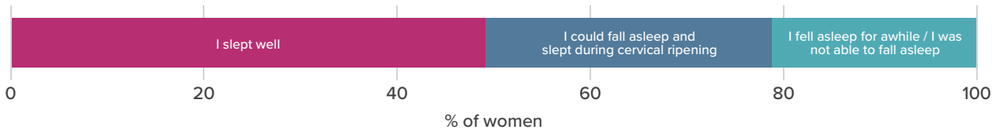
	All females		Females with previous CS		Females without previous CS	
	n	%	n	%	n	%
Vaginal	68	71.6	22	64.7	46	75.4
Cesarean section	27	28.4	12	35.3	15	24.6

The average number of dilators inserted was 3 (range: 2-5) and in most cases inserted dilators of Dilapan-S were in situ overnight. All 96 women completed the satisfaction questionnaire. 93.7% (89/93) evaluated the procedure of insertion of Dilapan-S as similar to other gynecological examinations or more unpleasant but still quite tolerable. Patient's soreness assessment of Dilapan-S insertion resulted in a mean pain score of 3.2 (0-10 point scale). 79% of all women were able to sleep without any problems or with only minor difficulties **(See Figure 1)**. Uterine contractions during cervical ripening phase were assessed as none, mild, or moderate in 90% of all women. Uterine hypertonus during preinduction was not recorded. Signs of fetal hypoxia did not occur on CTG trace during preinduction. A pH value of 7.10 and less from umbilical artery was found in 1 newborn (1.0%). Apgar score at 5th minute less than 7 was found in 1 newborn (1.0%). One case of postpartum metritis was reported after vaginal delivery in the subgroup with CS in previous history. Postpartum infectious complications in newborns were not reported. The extraction of Dilapan-S was assessed by physician as easy in 100% of patients. Rupture of membranes associated with insertion of Dilapan-S was not reported in any of the participating females.

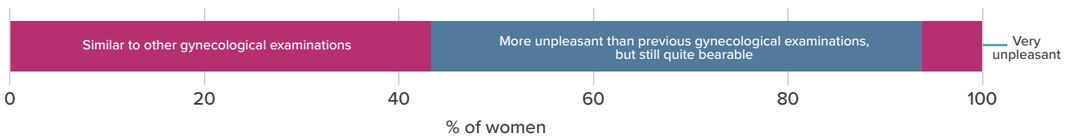
13 Efficacy and safety of the osmotic dilator Dilapan-S® for cervical ripening in women with/without Caesarean section

Figure 1: Patient satisfaction survey outcomes

A. Patient assessment of ability to sleep during cervical ripening



B. Patient assessment of Dilapan-S insertion



INVESTIGATOR CONCLUSIONS: Dilapan-S administered for cervical ripening prior to labor induction was effective concerning the increase of the Bishop score regardless of cesarean section in their medical history. 71.6% of all women delivered vaginally. The majority (93.7%) of all women evaluated the insertion of Dilapan-S as fully acceptable. 79% of all females were able to sleep without any or only minor problems. Use of Dilapan-S was not associated with occurrence of excessive uterine contractions, infections or other complications in all 96 cases.

14 The impact of the number of pieces of osmotic dilator Dilapan-S® used for cervical ripening on the course and outcome of labor

AUTHORS:
J. Záhumenský, L. Hruban, P. Janků, O. Šimetka, I. Michalec, R. Vlk, A. Toman, R. Doubek, K. Roušarová

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CONGRESS:
Poster presented at 13th World Congress in Fetal Medicine, June 29–July 3, 2014, Nice, France

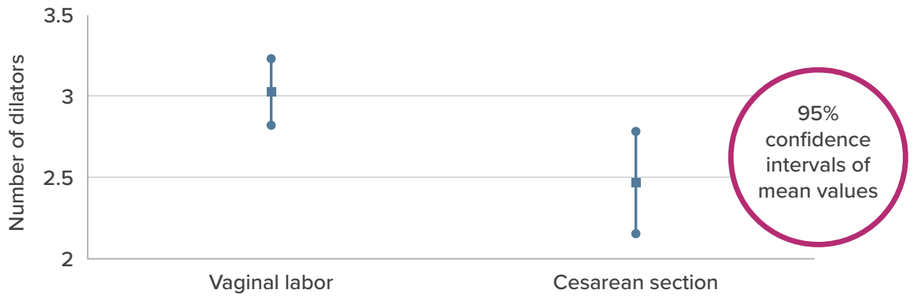
PURPOSE:
The objective of this study was to evaluate efficacy and safety of the synthetic osmotic dilator Dilapan-S for cervical ripening prior to labor induction according to defined criteria and to compare results in females with/without cesarean section in their medical history.

METHODS:
This study was an observational, prospective, multicenter data collection on the use of Dilapan-S performed between May 2013 and October 2013. 96 women at 36+ weeks' gestation with Bishop score <4 were included in the data analysis. 36.5% (35/96) had a cesarean section reported in their medical history, while the group of females without previous cesarean section involved 61 women (63.5%). Assessment of the primary objective and success of cervical ripening procedure was based on the Bishop (cervical) score. Safety data collection was focused on fetal hypoxia, uterine hypertonus, clinical signs of infection and other potential adverse effects related to the use of Dilapan-S. Answers about satisfaction from patient's questionnaire were also analyzed.

RESULTS:
A statistically significant difference in the mean values of the cervix score change between groups of females with 2 and 4 inserted dilators was confirmed (P=.002). The analysis also showed that there is a statistically significant difference in the mean values of number of inserted dilators between patients with subsequent vaginal delivery and cesarean section (P=.0019) **(See Figure 1)**. The number of inserted dilators did not appear to have an impact on pain during insertion and the women's ability to sleep and relax during the preinduction.

14 The impact of the number of pieces of osmotic dilator Dilapan-S® used for cervical ripening on the course and outcome of labor

Figure 1: A higher mean number of Dilapan-S dilators inserted led to a higher vaginal delivery rate vs cesarean section (*P*=.0019)



INVESTIGATOR CONCLUSIONS: The use of a higher number of Dilapan-S dilators was more efficient in terms of efficiency of cervical dilation and also in terms of achieving a vaginal birth. A higher number of inserted Dilapan-S dilators was not accompanied by more pain during their insertion or worsening of rest for women during preinduction. Achieving shorter preinduction time was not among the objectives of this study, but from the presented impact of the number of Dilapan-S dilators on Bishop score, we can assume that the introduction of a higher number of dilators could potentially lead to a shortening of the preinduction time.

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13. Vlk R, Hruban L, Janků P, et al. Efficacy and safety of the osmotic dilator Dilapan-SR for cervical ripening in women with/without Caesarean section. Poster presented at: 13th World Congress in Fetal Medicine; June 29-July 3, 2014; Nice, France.
14. Záhumenský J, Hruban L, Janků, et al. The impact of the number of pieces of osmotic dilator Dilapan-S® used for cervical ripening on the course and outcome of labor. Poster presented at: 13th World Congress in Fetal Medicine; June 29-July 3, 2014; Nice, France.

INPORTANT SAFETY INFORMATION

Dilapan-S® CERVICAL DILATOR

Indication for Use:

Dilapan-S® is for use by healthcare professionals trained in OB/GYN whenever cervical softening and dilation are desired, such as for cervical ripening during term labor induction or gynecological procedures that require cervical preparation.

Contraindication:

Dilapan-S® is contraindicated in the presence of clinically apparent genital tract infection.

Warnings & Precautions:

- Dilapan-S® is intended for single use only. **Do not** reuse, resterilize, reprocess, or use if primary packaging has been opened or damaged. Discard after use.
- Careful placement of the device is essential to avoid traumatic injury to the cervix or uterus (see Instructions for Use—Insertion). The device should not be left in place more than 24 hours. **Instruct patients to:** Report any excessive bleeding, pain, or temperature elevation, and to avoid bathing, douching, and intercourse. Patients should return to the physician for removal of Dilapan-S® at the indicated time and should be instructed not to attempt self-removal under any circumstances.
- Potential Complications/Risks: Twisting of device during removal may cause the device to break (see Instructions for Use—Removal). Complications may include: device entrapment and/or fragmentation, expulsion, or retraction; patient discomfort or bleeding; spontaneous rupture of membranes; spontaneous onset of labor; cervical laceration.

Storage & Handling:

Store between +15°C and +30°C and keep away from direct sunlight and high humidity.

Pleaes see Instructions for Use on pages 45-46.

medicem

DILAPAN-S® Hygroscopic Cervical Dilator

Instructions for Use

GENERAL INFORMATION

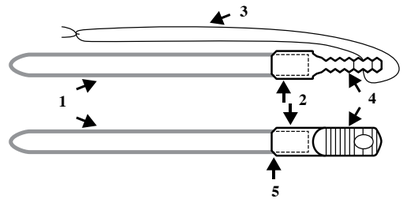
Content

A sterile hygroscopic cervical dilator packed in a printed composite primary peel-open pouch, a piece of Instructions for use.

The DILAPAN-S® is available in a box of 25 dilators and in the following dimensions: 4×65 mm, 4×55 mm, 3×55 mm.

Device description and performance

Synthetic hydrogel cervical dilator consists of the dilating part, the polypropylene handle and the marker string (see the figure below). The dilating part is manufactured from an anisotropic xerogel of AQUACRYL. The dilator is capable of increasing in diameter as it absorbs moisture from the genital tract. The marker string is tied securely to the handle of the DILAPAN-S®, and is provided to indicate its location.



1. Dilating part made of hydrogel
2. Collar
3. Marker string
4. Handle
5. Point of maximal insertion

Handling, transport, storage and waste management

Store between +15 °C and +30 °C.
Keep away from direct sunlight and high humidity.
Do not freeze.

The product, its waste materials and other consumables used during the procedure, should be disposed in accordance with local/national regulations.

Sterilization and expiration

The sterility of each device is guaranteed only when the primary packaging is unopened and undamaged.

The sterilization procedure that has been applied is marked on the label of the device – using irradiation.

INTENDED PURPOSE

Indications

The DILAPAN-S® is to be used wherever cervical softening and dilation is desired, some examples are:

- Cervical stenosis
  - Related to dysmenorrhea
  - Considered a possible cause of infertility
  - Resulting from cauterization or conization
- Placement and removal of intrauterine devices
- Induction of labor
- Radium placement
- Drainage of uterine cavity
- Endometrial biopsy
- Uterine curettage
- Suction aspiration cannula
- Operative hysteroscopy

Patient target group

The DILAPAN-S® is targeted for women indicated to labor induction or intrauterine procedure with necessary cervical ripening and/or dilation.

Intended users

The DILAPAN-S® is for use by healthcare professionals trained in obstetrics and gynecology only.

Contraindications

The DILAPAN-S® is contraindicated in the presence of clinically apparent genital tract infection.

WARNINGS

The DILAPAN-S® is intended for one-time use. Instructions for its use and handling are attached to minimize exposure to conditions that may jeopardise the product, patient or user.

Re-use / re-sterilization / reprocessing[1)] of the DILAPAN-S® single-use medical device may result in physical damage to the medical device, failure of intended use of the medical device, and illness or injury to the patient as a result of infection, inflammation and / or disease due to product contamination, infections and insufficient sterility of the product.

[1)] A process carried out on a used device in order to allow its safe reuse including cleaning.

Careful placement of the device is essential to avoid traumatic injury to the cervix or uterus and to avoid migration of the device either upward into the uterus or downward into the vagina.

The DILAPAN-S® may fragment during removal using incorrect technique. Fragmentation may result in pieces of the device being retained in the uterus. Carefully follow the Removal instructions.

Do not use if primary packaging has been opened or damaged.

Do not re-use, intended for one-time use.

Do not re-sterilize this device by any method.

Do not store at a temperature lower than +15 °C and higher than +30 °C.

Keep away from direct sunlight and high humidity.

Disposable, discard after use.

All instructions must be carefully read **prior to** using the DILAPAN-S®.

Caution: U.S. federal law restricts this device to sale by or on the order of a physician.

PRECAUTIONS

As with the use of any medical device, a careful evaluation and clinical judgement should be made by the healthcare professional before using the device for the procedure to decide on the benefit/risk ratio. Alternative treatment should be considered for patients with a pre-existing condition listed under contraindications above.

Treatment options and potential risks associated with using the DILAPAN-S® for planned procedure should be discussed with the patient before the procedure.
The patient should be instructed to report any excessive bleeding, pain, temperature elevation. The patient should be instructed to avoid bathing, douching and refrain from intercourse while the DILAPAN-S® is in place.

The patient should be instructed that it is necessary to return for removal of the DILAPAN-S® at the indicated time. Under no circumstances should the patient try to remove the DILAPAN-S® herself.

The device **should not** be left in place more than 24 hours.

When the dilator has been inserted during a procedure for termination of pregnancy, the procedure of termination of pregnancy should always be completed. Effect of termination the procedure on the fetus has not been clinically investigated.

Risks associated with the procedure

Twisting the device during its removal may cause the device to break.

In case of breakage, every attempt must be made to remove all fragments from the uterus. All fragments removed should be checked to ensure complete evacuation of the cavity. If in doubt, a hysteroscopy or ultrasound scan should be performed. The clinical effects of fragments retained in the genital tract are unknown.

Any cervical manipulation may cause a vaso-vagal reaction. The patient should be watched for evidence of any unusual pallor, nausea, vertigo or weakness. By remaining recumbent for 3 to 10 minutes these symptoms usually disappear.

Complications

The following complications may be associated with use of the DILAPAN-S® device, or may occur during the indicated procedure:

- Device entrapment
- Fragmentation or detachment of the handle
- Device expulsion
- Device retraction into the uterus
- Patient discomfort or bleeding during and/or after insertion
- Spontaneous rupture of membranes
- Spontaneous onset of labor
- Cervical laceration

USE

Examine the label of the unopened pouch and expiry date of the dilator.

Instructions for insertion

1. Insert a bivalve speculum and prepare the vagina and cervix with an antiseptic solution.
2. Remove the DILAPAN-S® from the pouch using sterile technique.
3. Moisten the DILAPAN-S® with sterile water or saline to lubricate the surface prior to insertion.
4. If necessary, use an appropriate technique to visualize the cervix and straighten the cervical canal for easier insertion of the DILAPAN-S®.

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5. Insert the DILAPAN-S® in the cervical canal gradually and without undue force. It is important that the DILAPAN-S® traverses the internal os. Do not touch the dilating part with a sharp instrument.
6. Do not insert the DILAPAN-S® past the handle. The border of the collar should rest at the external os. Do not insert the DILAPAN-S® into cervix further than the arrow indicates (see the figure above – 5. Point of maximal insertion).
7. More than one DILAPAN-S® may be inserted into the cervical canal as determined to be appropriate by the physician.
8. When using several dilators, repeat steps 2 to 4. As many dilators as needed to achieve the desired effect should be inserted. Specific number of pieces always depends on decision and clinical judgement of physician and indications.
9. Insert a gauze pad moistened with sterile water or saline to help keep the DILAPAN-S® in place, if needed.

Removal instructions

1. Vaginal packing is first removed, if used during the insertion procedure.
2. Carefully remove the DILAPAN-S® by grasping the handle or pulling the string. Do not twist[2)] the DILAPAN-S® during removal. Do not grasp the collar with forceps. Do not grasp the marker string with a sharp-edged instrument[3)].

[2)] Neither grasp the collar with forceps to remove the device nor twist handle when attempting to remove the device, as this may cause the device to break.

[3)] Do not grasp the marker string with a sharp-edged instrument to remove the device, as this may cause the string to tear.

When difficulties occur during removal of the device by pulling the string, do not use excessive force on the string to remove the dilator. Use a visualization technique to identify the cause of these difficulties and remove the dilator by grasping the handle.

Occasionally, it may be necessary to use forceps to grasp the DILAPAN-S® by the handle and exert steady traction for several minutes, while the uterus is stabilized by placing an atraumatic tenaculum through the anterior lip of the cervix.

Moisten the DILAPAN-S® with sterile water or saline thoroughly during removal, if the dilator has stuck to the tissue, or more dilators have stuck together.

In very rare cases the ballooning of the inserted DILAPAN-S® above and/or below the internal cervical os has been known to cause a "tight cervix" and make for difficult DILAPAN-S® removal. This is corrected by sliding a sequence of graduated sizes of metal dilators alongside the DILAPAN-S® and through the internal os until sufficient dilation takes place to allow easy withdrawal.

If the DILAPAN-S® has somehow migrated or been placed in a false passage, it may be located using ultrasound.

NOTE: The DILAPAN-S® is not radiopaque.

INTERACTIONS

Within clinical investigations with the DILAPAN-S®, a broad range of licenced medications have been administered during indicated procedures. No specific interactions between drugs / medical devices and the DILAPAN-S® have been identified to date. Using the DILAPAN-S® does not impose any specific limitations on standard medication administered in the context of the DILAPAN-S® indications. Information provided to particular medications should be followed properly.

External influences

No negative interactions between the DILAPAN-S® and external influences were observed. Desired interference include ultrasound waves that can be used for location of the inserted dilator.

TESTING OUTCOMES

Clinical

Clinical trials have not demonstrated any allergic reactions to the device. However, an allergic reaction could result from hypersensitivity to the components.

Clinical trials have not demonstrated any infections causally related to the DILAPAN-S®. However, in the presence of pathogens, contamination of the device during insertion is possible. Administration of antibiotic for infection prophylaxis should be considered prior to insertion of DILAPAN-S®.

Mechanical

The amount of dilation achieved depends on the amount of time in situ. The following is provided as a guide.

Time in situ (hours)	Expected Dilation (in mm)	
	One DILAPAN-S® (3 mm)	One DILAPAN-S® (4 mm)
2	7.2 – 8.3	7.8 – 10.0
4	8.4 – 9.5	10.0 – 11.2
6	9.0 – 10.0	10.1 – 12.5
24	9.6 – 11.3	12.7 – 14.6

CONTACTS AND VIGILANCE

Please report incidents of death to the FDA or serious injury to your distributor (USRegulatory@medicem.com) or to the manufacturer (technology@medicem.com) in relation to the DILAPAN-S®.

Please report any potential or actual product deficiencies, and product quality issues associated with the use of the DILAPAN-S® directly to your distributor (USRegulatory@medicem.com) or to the manufacturer (technology@medicem.com).

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Initial Importer, Distributor and US Agent:
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Liability

The manufacturer holds no liability for any side effects or resulting damages, losses or costs that may arise as a result of the incorrect handling or use of the device.

CE 2797

TABLE OF USED SYMBOLS

	Keep in a dry place
	Keep away from sun
	Store at 15 – 30 °C
	Sterile, Sterilized using irradiation
	Do not re-use
°C	Degrees of Celsius
	Caution, Consult accompanying documents
	Do not resterilize
	Do not use if package is damaged
	Consult instructions for use
mm	Millimeter
	Batch number
	Expiration date
	Date of manufacture
	Manufacturer
QTY	Quantity
pc / pcs	Piece(s)