



## Effects of Vaginal pH on the Efficacy of Vaginal Misoprostol for Induction of Midtrimester Abortion

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### ABSTRACT

To evaluate the effect of vaginal pH on the efficacy of misoprostol for induction of midtrimester abortion. The purpose of this study was to evaluate the influence of vaginal PH on the efficacy and side – effects of misoprostol for the induction of midtrimester abortion. The study compared 100 women, with gestational age of 14-26 weeks, with a missed abortion as an indication aboration induction. On admission, the vaginal pH was measured and the patients were randomly assigned into two groups: (A) those with  $pH < 5$  ( $n = 66$ ), and (B) those with  $pH \geq 5$  ( $n = 34$ ). All of the women received intravaginal misoprostol tablets moistend with 3 ml of 3% acetic acid. Two hundred  $\mu g$ , every 4 hrs for a maximum of 5 doses within 24 hrs were administered. If the patient did not have adequate uterine contractions, the same regimen was repeated over the following 24 hrs and if no response was achieved, this was considered a failare of therapy. All patients aborted within 48 hrs. A significant positive correlation between vaginal pH and the misoprostol application- abortion interval was significantly shorter in group A compared to group B (12.68 vs 23.98,  $P < 0.001$ , with abortion rates at 24 hrs being 100% and 41.2% respectively. Moreover, a significantly lower dose of misoprostol was used in group A than B (3.50 Vs 5.6) and there was no severe maternal complication in the present study. The number of patients with fever or blood loss or abdominal pain was not significant positive correlation, but in group A showed lower incidence. Group B showed a higher incidence of neusea and vomiting. In both group, there was no blood transfusion, need for curettage, or any serious complication such as uterine rupture or cervical laceration. Vaginal pH influences the efficacy of misoprostol administered vaginally for the induction of midtrimester abortion. The presence of the relation- ship, despite premoistening with an acidi fying agent, suggests that the effect of vaginal pH might extend beyond affecting the pharmacokinetics of the drug.

**Keywords:** Acetic acid, Misoprostol, Second trimester pregnancy termination, Vaginal PH

### INTRODUCTION

In the United States in 2000, a total of 857,475 cases of induced abortions have been reported, 60% of induced abortions had been charged with in the first 8 weeks of pregnancy and 88% of abortions in the first 12 weeks of pregnancy (1). Most legal abortions occur before 13 weeks after menstruation (2-7). Many attempts have been made throughout history to find a natural material as a factor of abortion induction, but in most cases, instead of abortion severe systemic disease or maternal death occurred. Today, there are only a few drugs that cause abortion without risk (3, 8-11). Three drugs studied for early medical abortion in wide level: they are Anti-progestin Mife Preston, Anti- metabolite methotrexate and prostaglandin misoprostol. These drugs by increasing the strength of uterine contraction are caused induced abortion (4, 12-15). Abortion in the higher gestational age is associated with greater risks. The complications of abortions doubly increased with gestational ages more than 14 weeks (5, 16-19).

So far, different methods have been used for abortion in the second trimester of pregnancy, including D & E, oxytocin infusion and injection of saline or urea into the amniotic fluid (6, 20-23). One of the common methods for inducing abortion in the second trimester of pregnancy is prescription the prostaglandin in to the vaginal (6, 7, 24-28).

Misoprostol is a synthetic prostaglandin analogue E1 that is widely is used to Cervix ripening in the induction of abortion and also is used to induce labor. This medicine is designed for comestible use as tablets, but in some cases it can also be used as a vaginal (7-9, 29-32).

The vaginal misoprostol absorption is different for various patients. The effect of wetting the tablets with water or Salin to increase the solubility of termination of pregnancy has been proven in the first quarter (9, 33-37). Studies have shown that the success rate of abortion ways with misoprostol is fully associated with plasma drug levels and to achieve to the highest plasma levels, is very important that can create an environment in the vagina that caused the greatest solubility and absorption of the drug. Some studies have shown that misoprostol dissolves better in an acidic environment; in addition to, it has suggested that possibly using the pills to create acidic environment of the vagina such as citric acid tablets, along with misoprostol pills may increase our success in induction the abortion or childbirth (10, 11, 38, 39). Therefore, this study was conducted to identify the best conditions for the functioning of misoprostol.

### MATERIALS AND METHODS

This study was done on patients that were hospitalized in Imam Khomeini and Razi hospital with missed abortion in the second trimester (14 to 26 weeks) in Ahvaz. The time of performing this project was from June to December 2009.

All patients with missed abortion were hospitalized in hospital and were evaluated for entering to the study. Patients selected based on inclusion and exclusion criteria of the study.

Criteria of inclusion to the study: singleton pregnancy with gestational age at 26-14 weeks, Cervix with the normal appearance without dilatation and effacement on physical examination, the absence of uterine contractions and normal coagulation tests (PTT, PT). Bloody vaginal discharge or vaginal bleeding or rupture of the membranes or doubt to the infectious abortion, medical diseases such as hypertension or mellitus diabetes, cerclage or previous trauma of Cervix, lacerations of the cervix, previous failure for the present pregnancy termination and contraindications for medical abortions, uterine scars caused by previous surgeries or caesarean section or myomectomy, that has encroached to the uterine vesicular.

Before the examination the vagina by finger, speculum examination is performed and pH of the vagina is evaluated with paper indicator paper. Indicator paper with the help of forceps inserted in the upper part of the vagina until it gets wet, changing the color of the paper compared with the certain paints and vaginal pH is determined.

Based on vaginal pH, patients are divided in to two groups A ( $\text{pH} < 5$ ) and B ( $\text{pH} \geq 5$ ). After vaginal examination, 200 mcg misoprostol with 3 ml 3% acetic acid is wet and is inserted in the vagina with a finger. This work is repeated every 4 hours up to maximum 5 times in 24 hrs to happen the abortion: after uterine found contractions then is not prescribed any drug. When abortion happened in 24 hrs, the study will be completed. If the uterus did not find proper contractions to 8 hours after prescription the fifth dose of drug, similar regime will be repeated for the next 24 hrs. And if still there was no response, it knows as a failure of the treatment and another treatment is used based on the clinical judgment of the doctor.

Patient's vital signs, including temperature, the numbers of pulse and blood pressure are measured every 4 hours. All patients were monitored continuously in the term of the onset of uterine contractions, discharge pregnancy products; side effects of the treatment with misoprostol include vomiting, diarrhea, fever, lower abdominal pain and vaginal bleeding. Need to the curettage is also recorded and patients after discharging with the pelvic ultrasound were been following by referring to the women's clinic.

For analysis of the results, at first by using of statistical methods the studied variables were explained. In this section amounts of appearing the symptoms associated with confidence limitations were calculated and then by using statistical tests, qualitative and quantitative variables were compared between the two groups. A significant level was considered for the above 0.05 tests. Data analysis was performed by using of SPSS16.

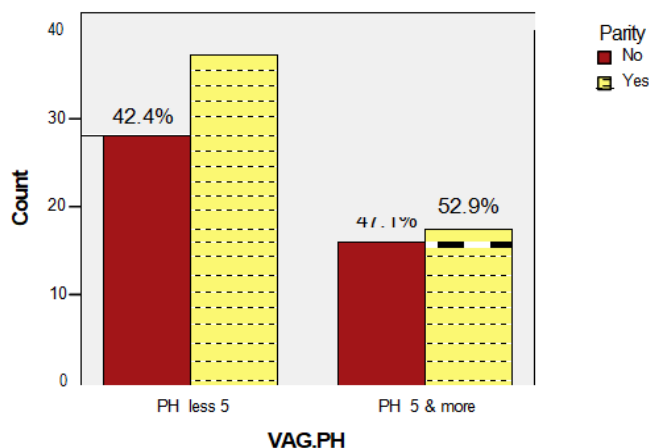
**RESULTS**

Overall, 100 women in the second trimester of pregnancy due to missed abortion, were candidate for the therapeutic abortion based on measuring vaginal pH, were randomly divided into two groups with vaginal pH less than 5 and vaginal pH greater than or equal to 5, and were compared together post treatment (Tables 1-3, Figs. 1-12).

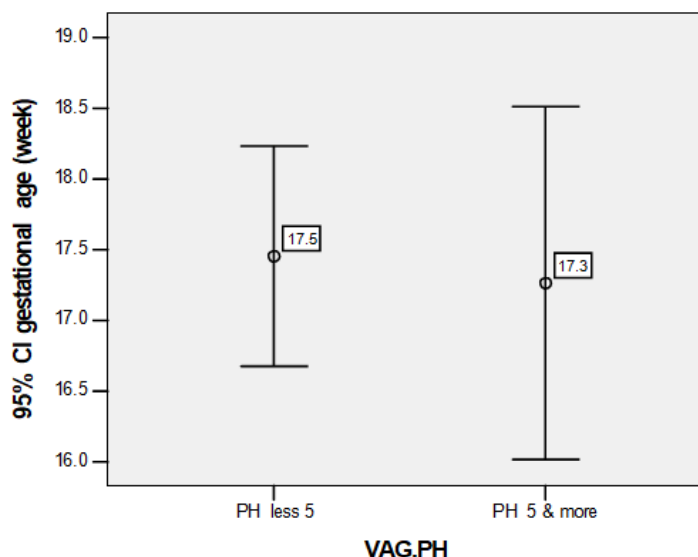
**Table 1. Comparison of age average between the two groups**

Standard deviation	Average	PH	number
419 ± 6	26.27	<5	64
32 ± 6	62.26	≥ 5	34

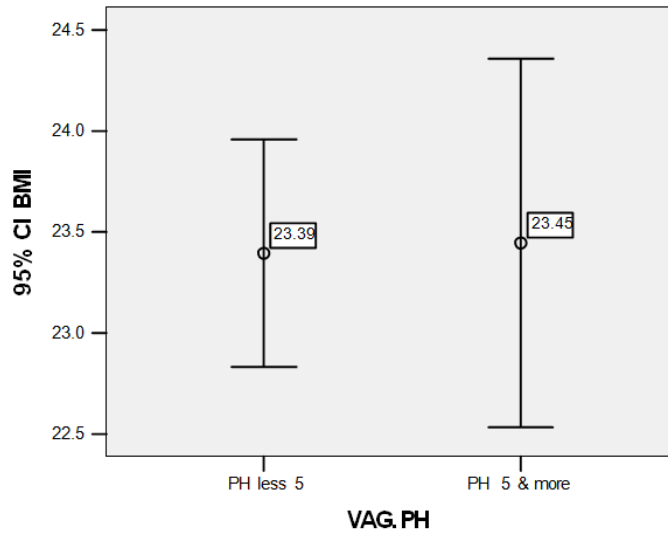
**Bar Chart**



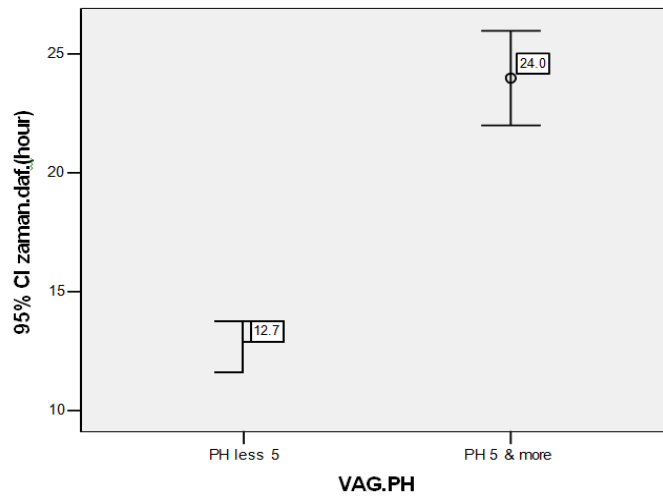
**Fig. 1. Comparison of parity between the two groups**



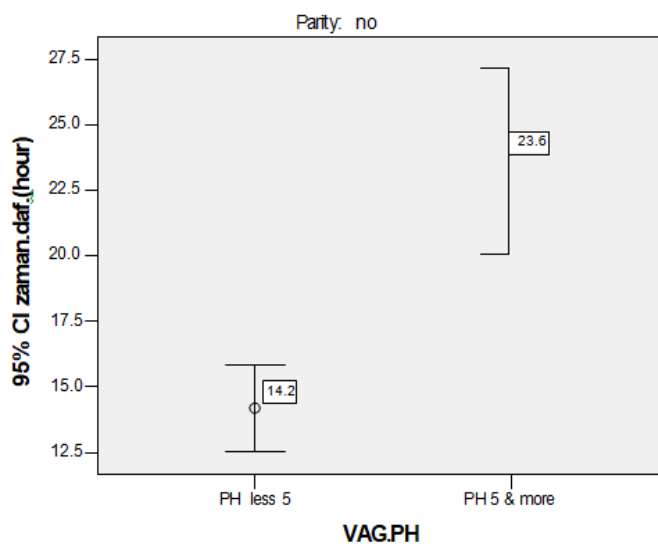
**Fig. 2. Distribution of pregnancy age in the two groups (by week)**



**Fig. 3. Comparison of average BMI in the two groups**



**Fig. 4. Comparison of the time-abortionof fetus in two groups**



**Chart 5. Comparison of the average time that it takes to abortion the fetus among nulliparous women**

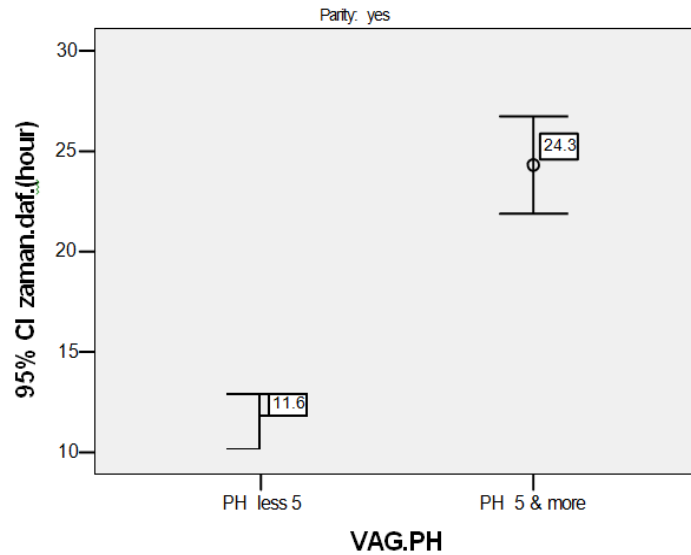


Fig. 6. Comparison of the average time of fetus abortion among multiparous women between two groups

Table2. Comparison of the average time between the fetus abortion between the two groups within 12, 24 and 48 hrs

Successful Aborti-with 48	Successful Aborti- with 24	Successful Aborti- with 12	
66 (100%)	66 (100%)	26 (39.4%)	< 5 PH
34 (100%)	14 (41.2%)	(0%)	≥ 5 PH

Table 3. Comparison of the average dosage intake between the two groups

PH	number	Standard deviation	The largest and number smallest
< 5	67.766	55.261	200 -1000
≥ 5	82.1285	263	600 - 1600

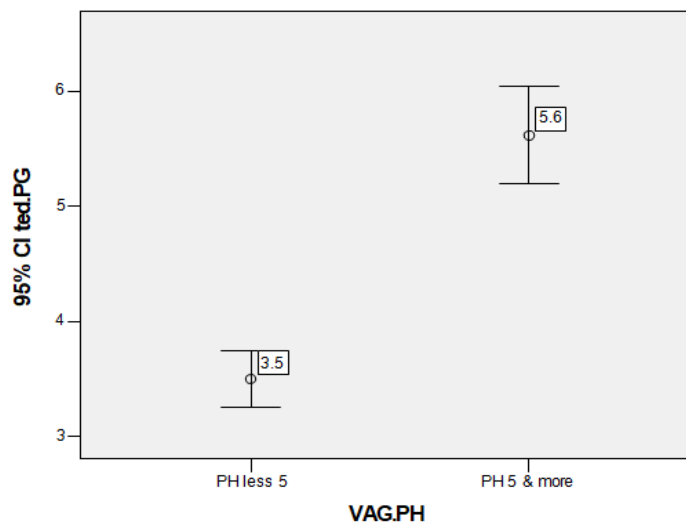


Fig. 7. Comparison the average number of pills between the two groups

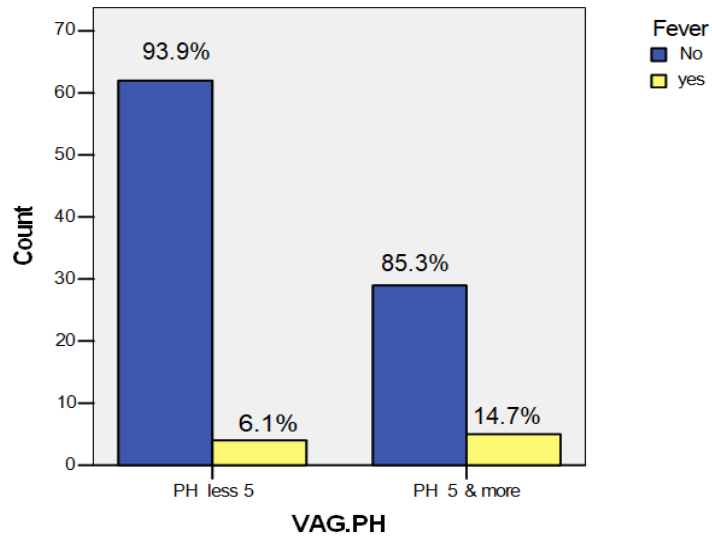


Fig. 8. Comparison of fever between the two groups

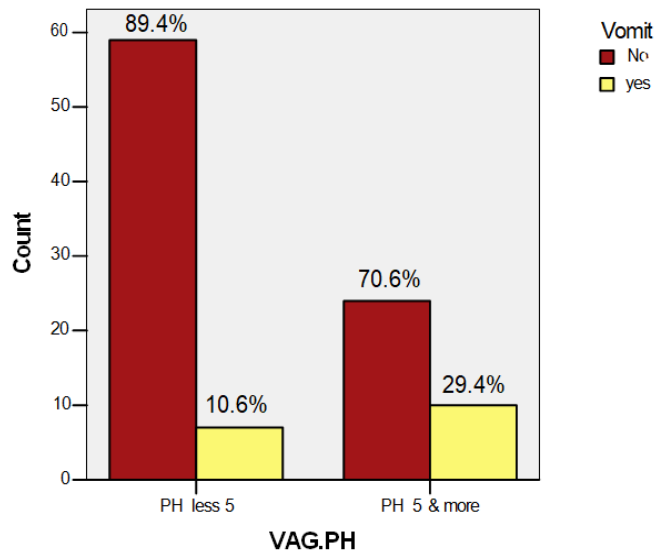


Fig. 9. Comparison of nausea and vomiting in both groups

Bar Chart

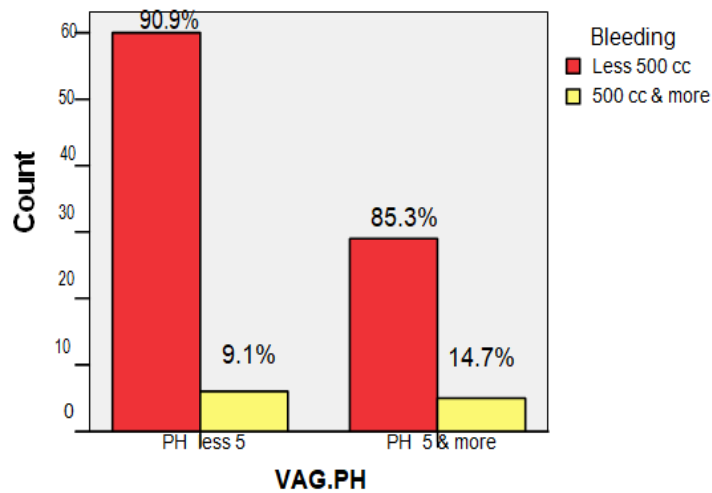


Fig. 10. Comparison of the incidence rates of bleeding between the two groups

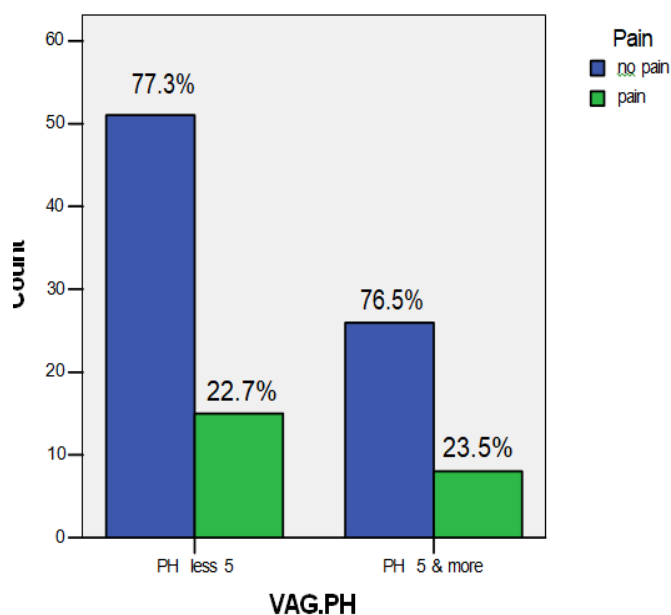


Fig. 11. Comparison the incidenc rates of abdominal pain between the two groups

Bar Chart

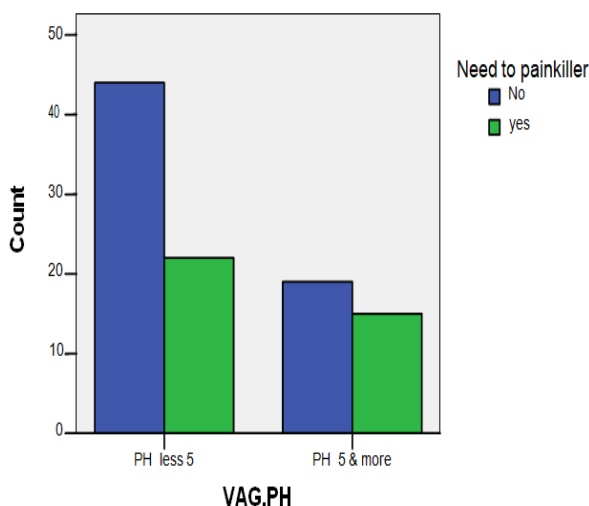


Fig. 12. Comparison of the need for painkillers between the two groups

None of the groups showed diarrhea, abortion and the need for blood transfusions. There was a direct and severe correlation between vaginal PH and the time it takes from the drug percription to the induction, in such way that the PH elevation increases the time needed for disposal.

**DISCUSSION**

In this study was shown that there is a positive relationship between the PH of the vagina and the time of disposal specified in the second quarter missed abortion.

Use of misoprostol in women with PH <5 has accompanied with the shortest and the most disposal rates compared with women with amount of PH ≥ 5 (P< 0.001). In a study that was done in Cairo, were obtained similar results (12). Similar the Cairo study in women with PH <5 vagina, it was needed to lower numers and doses of prostaglandin compared with women with PH ≥ 5, P <0.001.

The effectiveness of perscription of the vaginal misoprostol to induce the labor and to soften the cervix has been

linked in previous studies with PH vagina (13, 14).

Improve the effectiveness of wetting misoprostol tablets with 1 ml of acetic acid 3%, (PH= 2.5) in previous studies, was a guidance for future studies (15) and also for our study. However, in some studies also found no difference in wetting misoprostol and without wetting with normal saline (16) and it is recommended that vaginal PH effect on the efficacy of prescription the vaginal misoprostol, should go beyond the Farmaktic drug.

In this study, in terms of the incidence rate of nausea and vomiting, there was statistically significant differences between the two groups (P= 0.018 and in the group of  $\text{PH} \geq 5$ , nausea and vomiting was higher. However, in another study that was done by Karim H in  $\text{PH} < 5$  the incidence of nausea and vomiting was higher. However, there was no statistical difference (P = 0.19) (12).

In this study, in the group that  $\text{PH} < 5$  was associated with less bleeding, but there was no statistically significant difference between the two groups P = 0.5.

In terms of the incidence rates of abdominal pain (P= 0.9) and the need for painkiller medicine and the dose of using painkiller medicine (P= 0.06), there was difference between the two groups but it was not statistically significant. In this study, with low-dose misoprostol uterine rupture did not occur but in studies that have been done with higher doses of misoprostol in the past two decades in those who had uterine scar, uterine rupture had occurred (17-19).

In several studies have been reported, the second quarter missed abortions compared with abortions with live fetuses were needed to lower doses of misoprostol and the time of disposal was shorter (20, 22).

## CONCLUSION

To wet the misoprostol with acetic acid facilitated the dissolve of the pills in this study, but the effectiveness of misoprostol for second trimester, is depending on the PH of the vagina and is recommended that vaginal PH effect on the efficacy of vaginal misoprostol is beyond the Farmakoktic medicine and more studies are needed to explain this low vaginal PH effect on the efficacy of vaginal misoprostol.

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