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Clinical efficacy and safety of reformulated Acidosalus® vaginal pessaries compared with Bioapigyn® pessaries in the treatment of vulvovaginal disorders: A randomized comparative study

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Abstract: Vulvovaginal disorders associated with elevated vaginal pH commonly present with vaginal discharge, unpleasant odor, itching, burning, dryness, and dyspareunia. Medical devices acting through physical mechanisms, such as restoration of an acidic vaginal microenvironment and formation of a protective mucosal barrier, represent an important non-pharmacological treatment option. Acidosalus® vaginal pessaries were reformulated by replacing live probiotic bacteria with a non-viable probiotic yeast (*Kluyveromyces marxianus fragilis* B0399 TN), necessitating renewed clinical evaluation in accordance with Regulation (EU) 2017/745. To evaluate the clinical efficacy and safety of reformulated Acidosalus® pessaries compared with Bioapigyn® pessaries and to contextualize the results with previously published data on the earlier Acidosalus® formulation. A prospective, randomized, comparative clinical study was conducted in adult women with nonspecific or mixed vulvovaginal disorders associated with increased vaginal pH. Participants were treated once daily for seven consecutive days with either Acidosalus® or Bioapigyn® pessaries. Efficacy outcomes included patient self-assessment of symptoms, investigator assessment, vaginal pH measurement, and evaluation of vaginal purity by native wet mount microscopy. Safety was assessed by monitoring adverse events and local tolerability. Acidosalus® pessaries reduced vaginal discharge by 82.4%, unpleasant odor by 91.7%, itching by 88.9%, burning by 85.7%, and vaginal dryness by 90.0%. Vaginal pH decreased by 12.3%, and normalization of vaginal flora was achieved in 92.5% of patients. Bioapigyn® pessaries demonstrated comparable efficacy, with symptom reductions ranging from 80.0% to 100%, a 13.0% decrease in vaginal pH, and normalization of vaginal purity in 82.5% of patients. Overall, 85% of participants achieved clinical cure and 15% clinical improvement. No clinical failures or safety concerns were reported. Reformulated Acidosalus® vaginal pessaries are safe and clinically effective in the treatment of vulvovaginal disorders associated with increased vaginal pH, demonstrating efficacy and safety comparable to an established medical device and consistent with previously reported data, thereby supporting their use in accordance with MDR (EU) 2017/745 requirements.

1. Introduction

Vulvovaginal disorders are among the most common conditions encountered in gynecological practice and represent a significant burden on women's quality of life. Typical symptoms include vaginal discharge, irritation, itching, burning, malodor, vaginal dryness, and dyspareunia. A common pathophysiological feature underlying many of these conditions is an elevation of vaginal pH above the physiological acidic range, which disrupts the vaginal microenvironment and facilitates colonization and overgrowth of pathogenic or opportunistic microorganisms. In healthy women of reproductive age, vaginal pH is maintained between approximately 3.6 and 4.5 through lactic acid production by vaginal lactobacilli and epithelial cells. This acidic milieu represents a key defense mechanism, limiting microbial growth and adhesion. Numerous studies have demonstrated a strong association between elevated vaginal pH and bacterial vaginosis as well as other vulvovaginal disorders (**Larsen & Monif, 2001; Boskey et al., 1999; Klebanoff et al., 1991**). In peri- and postmenopausal women, estrogen deficiency contributes to reduced glycogen content in vaginal epithelial cells, diminished lactic acid production, and a consequent increase in vaginal pH, further increasing susceptibility to symptoms and mucosal damage (**Milsom et al., 1993; Caillouette et al., 1997; Roy et al., 2004**).

Conventional pharmacological treatments for vulvovaginal infections are primarily directed toward eradication of specific pathogens. While often effective in the short term, such treatments do not directly restore the vaginal

microenvironment or mucosal barrier and may therefore be associated with frequent recurrence, particularly in conditions such as bacterial vaginosis. This has led to increasing interest in non-pharmacological medical devices that act through physical or physicochemical mechanisms. Acidosalus® vaginal pessaries are medical devices intended for local vaginal use, designed to alleviate symptoms of vulvovaginal disorders associated with increased vaginal pH through exclusively physical mechanisms, including the formation of a protective mucosal coating and restoration of an acidic vaginal microenvironment. A previous formulation containing live probiotic bacteria demonstrated high clinical efficacy and safety in a randomized comparative clinical study (Oreščanin et al., 2019). In the context of regulatory transition to Regulation (EU) 2017/745 (MDR), the device was reformulated by replacing live probiotic bacteria with a non-viable probiotic yeast, while maintaining the same intended purpose and mode of action.

In contrast to pharmacological clinical trials, where placebo or untreated control groups are typically required, clinical investigations of medical devices are appropriately designed using active comparators representing current clinical practice, in accordance with MDR (EU) 2017/745 and MEDDEV 2.7/1 rev. 4 principles. Such an approach enables a clinically relevant evaluation of device performance under real-use conditions. Therefore, the present study was designed to evaluate the clinical efficacy and safety of reformulated Acidosalus® vaginal pessaries in comparison with Bioapigyn® vaginal pessaries, an established medical device with a comparable intended purpose, mode of action, and site of

application, and to contextualize the findings with previously published clinical data on the earlier Acidosalus® formulation.

2. Material and Methods

2.1. Study design and setting

This study was designed as a prospective, randomized, comparative clinical investigation conducted at a single clinical center (Findri Guštek Healthcare Institution, Ninska 5a, Sesvete, Croatia) between June and November 2022. The study was performed in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice (ICH-GCP E6-R2). The study protocol, patient information sheet, and informed consent form were reviewed and approved by the Ethics Committee of the Findri Guštek Healthcare Institution, consisting of five members (Štefica Findri Guštek, Zvezdana Štaba, Ivana Čankar, Ivan Vlahek, and Branko Guštek). All participants provided written informed consent prior to enrollment. Regulatory approval was obtained under EudraCT number 2019-001054-26.

2.2. Patients

Adult women with nonspecific or mixed vulvovaginal disorders were identified and invited to participate in the study based on medical indication and their medical history, in accordance with predefined inclusion and exclusion criteria. Inclusion criteria comprised age ≥ 18 years, presence of vulvovaginal symptoms associated with increased vaginal pH, suitability for local treatment, and provision of written informed consent. Exclusion criteria included clinically suspected specific genital infections requiring systemic therapy, pregnancy or lactation, recent

gynecological surgery or childbirth, recent use of topical or systemic antimicrobial therapy, known hypersensitivity to any component of the investigational devices, and participation in another clinical study. A total of 100 patients were screened, of whom 80 met all inclusion and exclusion criteria and were enrolled in the study. Patients were randomized in a 1:1 ratio to receive either Acidosalus® vaginal pessaries or Bioapigyn® vaginal pessaries (40 patients per group).

2.3. Investigational medical devices and treatment regimen

Acidosalus® vaginal pessaries are homogeneous solid formulations of characteristic herbal odor and yellowish color, packaged in blisters (2.7 g each). They are composed of cocoa butter (*Theobroma cacao* seed butter), hydrogenated coco-glycerides (Whitepsol E75), beeswax (*Cera alba*), macerate of St. John's wort (*Hypericum perforatum* L.), propolis (propolis extract), apple cider vinegar (*Acetum mali*), tamanu oil (*Calophyllum oleum*), essential oils of Australian tea tree (*Melaleuca alternifolia*), palmarosa (*Cymbopogon martinii*), and garlic (*Allium sativum*), beta-glucan (1,3- β -glucan from oats), probiotic yeast (*Kluyveromyces marxianus fragilis* B0399 TN), inulin, and lactic acid (*Acidum lacticum*). Bioapigyn® vaginal pessaries are homogeneous solid formulations of characteristic herbal odor and light yellow color, packaged in blisters (3 g each). A detailed description of the product has been previously published (Oreščanin et al., 2019).

Participants administered one vaginal pessary daily, preferably at bedtime, in accordance with the instructions for use.

The treatment duration was seven consecutive days. Participants were instructed not to use any other local vaginal products during the study period.

2.4. Clinical assessments

Clinical efficacy was evaluated at baseline and after completion of treatment using patient self-assessment of symptoms (vaginal discharge, unpleasant odor, itching, burning, vaginal dryness, and dyspareunia), investigator assessment of clinical signs, measurement of vaginal pH, and evaluation of vaginal purity by native (wet mount) microscopy. Clinical efficacy was categorized as clinical cure, clinical improvement, or clinical failure based on predefined criteria incorporating patient-reported symptoms, investigator findings, vaginal pH, and vaginal purity (Table 1).

Clinical cure was defined as complete resolution or marked improvement of signs and symptoms, normalization of vaginal purity (Grade I), and a decrease in vaginal pH of at least 10% compared to baseline values. Specifically, symptoms scored as mild (1) or moderate (2) at baseline had to be absent (score = 0) at follow-up, while symptoms scored as severe (3) had to decrease to a score of 0 or 1. Investigator-assessed signs present at baseline (score = 1) had to be absent (score = 0) at follow-up.

Clinical improvement was defined as a reduction in the number and/or severity of signs and symptoms, accompanied by a decrease in vaginal pH of 1–10% and partial improvement in vaginal purity, without fulfilling all criteria for clinical cure. Clinical failure was defined as absence of improvement in signs and symptoms, vaginal pH, or vaginal purity.

2.5. Safety assessment

Safety and tolerability were assessed throughout the study by monitoring the occurrence of adverse events, local irritation, allergic reactions, worsening of baseline symptoms, and the emergence of new symptoms.

All safety-related observations were recorded during the treatment period and at the follow-up assessment.

2.6. Statistical analysis

Statistical analysis was performed using the STATISTICA 12.0 software package. The required sample size was calculated using power analysis. Frequencies and percentages were calculated for categorical variables using frequency tables. Differences between groups of categorical variables were assessed using the χ^2 test.

Descriptive statistical parameters were calculated for continuous variables. The Shapiro–Wilk test was used to assess the normality of distribution, while Levene's test was used to evaluate the homogeneity of variances. For normally distributed continuous variables, differences between two groups (baseline and post-treatment values) were analyzed using the t-test. Differences among three or more groups were assessed using analysis of variance (ANOVA), followed by the Newman–Keuls post hoc test. Prior to statistical analysis, logarithmic transformation was applied to variables that deviated from normal distribution.

Table 1. Criteria for evaluation of clinical efficacy based on patient-reported symptoms, investigator-assessed signs, vaginal pH, and vaginal purity.

Signs and symptoms reported by patient (self-assessment) (Score – none 0, mild 1, moderate 2, severe 3)			Clinical efficiency at second visit Clinical cure (C): score 0 for initial values 1 and 2; score 0-1 for initial values 3 Clinical improvement (I): decrease in value but does not meet the conditions for clinical treatment Clinical failure (F): no decrease in initial values
	First visit	Second visit	
Vaginal discharge			
Unpleasant odor			
Itching			
Burning			
Vaginal dryness			
Dyspareunia			
Total			
Investigator-assessed signs/symptoms (score – absent 0, present 1)			Clinical cure (C): score 0 for initial value 1 of all signs/symptoms Clinical improvement (I): score 0 for initial values of 1 for at least one sign/symptom Clinical failure (F): no decrease in initial values
Edema			
Erythema			
Excoriation			
Erosion			
Vaginal discharge			
Total			
pH value of vaginal secretion expressed numerically			Clinical cure (C): pH value lower than the baseline by at least 10% Clinical improvement (I): pH value lower than baseline between 1% and 10% Clinical failure (F): no decrease in initial values
pH			
Vaginal purity (I-normal vaginal flora; II - vaginal flora disorder)			Clinical cure (C): the initial level of purity II at the control examination is improved to I Clinical improvement (I), initial degree of purity II at the follow-up examination, the finding has improved, but it is not of degree I Clinical failure (N): the initial level of purity II remains II at the follow-up examination
Vaginal purity			

3. Results and Discussion

3.1. Acidosalus® pessaries

The age of patients treated with Acidosalus® pessaries ranged from 25 to 81 years (49.8 ± 15.2 years). The number of childbirths ranged from 0 to 6 (1.6 ± 1.2), and the number of miscarriages from 0 to 2 (0.1 ± 0.4). The majority of participants had completed secondary education (62.5%). A total of 57.5% were married, and 75% reported having one sexual partner in the previous 12 months. Most participants (85%) did not use contraceptives. The predominant dietary pattern was boiled food (85%). A total of 77.5% of participants were non-smokers. Occasional alcohol consumption was reported by three participants, while one participant reported regular alcohol consumption. No use of illicit substances was reported.

A total of 27.5% of participants reported the use of dietary supplements, most commonly vitamins and minerals. Allergies were reported by 30% of patients, while 27.5% had chronic diseases. Three patients (7.5%) were receiving hormone replacement therapy, and 25% had undergone medical irradiation within 30 days prior to the study. Concomitant medication use was

reported in 40% of participants. In the Acidosalus® group, treatment resulted in a pronounced improvement in all assessed clinical parameters. Compared to baseline, vaginal discharge decreased by 82.4%, unpleasant odor by 91.7%, itching by 88.9%, burning by 85.7%, and vaginal dryness by 90.0% (Table 2). A significant reduction in clinical signs was also confirmed by the Principal Investigator (Table 3). Edema and erythema resolved completely, while vaginal discharge and total score decreased from 0.9 ± 0.3 to 0.1 ± 0.2 and from 1.5 ± 0.7 to 0.1 ± 0.2 , respectively. Vaginal pH decreased significantly from 5.7 ± 0.8 to 5.0 ± 0.6 (12.3%), indicating restoration toward the physiological acidic range. Normalization of vaginal microflora, defined as first-degree vaginal purity on native wet mount microscopy, was achieved in 92.5% of patients. Overall clinical outcome assessment showed clinical cure in 85% of patients and clinical improvement in 15%, with no cases of clinical failure. No adverse events, local intolerance, worsening of symptoms, or emergence of new symptoms were reported, confirming excellent safety and tolerability.

Table 2. Mean values $\pm$ standard deviations of patient-reported symptoms of vulvovaginal disorders at baseline and after treatment with Acidosalus® pessaries, with corresponding t-test results.

Signs/symptoms	Initial	Final	Decrease (%)	t	p
	$\bar{X} \pm SD$	$\bar{X} \pm SD$			
Vaginal discharge	1.7 ± 0.9	0.3 ± 0.6	82.4	8.2	<0.0001*
Odour	1.2 ± 1.2	0.1 ± 0.2	91.7	5.7	<0.0001*
Itching	0.9 ± 1.1	0.2 ± 0.5	88.9	3.7	0.0005*
Burning	0.7 ± 1.1	0.2 ± 0.5	85.7	2.6	0.0106*
Vaginal dryness	1.0 ± 1.2	0.1 ± 0.3	90.0	4.6	<0.0000*
Total score	5.5 ± 2.7	0.7 ± 1.1	92.9	10.4	<0.0000*

*Statistically significant at $p < 0.05$.

Table 3. Mean values $\pm$ standard deviations of investigator-assessed signs and symptoms of vulvovaginal disorders at baseline and after treatment with Acidosalus® pessaries, with corresponding t-test results.

Signs/symptoms	Initial	Final	Decrease (%)	t	p
	$\bar{X} \pm SD$	$\bar{X} \pm SD$			
Oedema	0.2 $\pm$ 0.4	0.0 $\pm$ 0.0			
Erythema	0.3 $\pm$ 0.5	0.0 $\pm$ 0.0			
Excoriation	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0			
Erosion	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0			
Vaginal discharge	0.9 $\pm$ 0.3	0.1 $\pm$ 0.2	88.9	14.0	<0.0001*
Total score	1.5 $\pm$ 0.7	0.1 $\pm$ 0.2	93.3	12.1	<0.0001*
Vaginal pH	5.7 $\pm$ 0.8	5.0 $\pm$ 0.6	12.3	4.4	<0.0001*

*Statistically significant at $p < 0.05$.

3.2. Bioapigyn® pessaries

The age of patients treated with Bioapigyn® pessaries ranged from 19 to 76 years (42.5 ± 15.0 years). The number of childbirths ranged from 0 to 4 (1.5 ± 1.2), and the number of miscarriages from 0 to 2 (0.2 ± 0.5). The majority of participants had completed secondary education (75%). A total of 62.5% were married, and 92.5% reported having one sexual partner in the previous 12 months. Most participants (95%) did not use contraceptives. The predominant dietary pattern was boiled food (87.5%). A total of 30 out of 40 participants were non-smokers. Alcohol consumption was reported by three participants, while two participants reported occasional use of illicit substances.

A total of 30% of participants reported the use of dietary supplements, most commonly vitamins. Allergies were reported by 45% of patients, while 20% had chronic diseases (e.g., hypertension and diabetes), and these patients were receiving regular therapy. One patient was receiving hormone replacement

therapy, and six patients had undergone medical irradiation within 30 days prior to the study. Concomitant use of medicinal products or medical devices was reported in 17.5% of participants.

According to patient self-assessment (Table 4), after 7 days of treatment with Bioapigyn® pessaries, all symptoms of vulvovaginal disorders decreased significantly, including the total score, which decreased from 5.1 ± 2.2 to 0.8 ± 1.1 . Symptom reduction ranged from 80.0% (vaginal dryness) to 100% (odor and itching), while the total score decreased by 84.3%.

A significant reduction in clinical signs was also confirmed by the Principal Investigator (Table 5). Edema, erythema, erosion, and vaginal discharge resolved completely, while the total score decreased from 1.4 ± 1.0 to 0.1 ± 0.3 (92.9%). Vaginal pH decreased significantly from 5.4 ± 0.8 to 4.7 ± 0.6 (13%), indicating restoration toward the physiological acidic range.

Table 4. Mean values $\pm$ standard deviations of patient-reported symptoms of vulvovaginal disorders at baseline and after treatment with Bioapigyn® pessaries, with corresponding t-test results.

Signs/symptoms	Initial	Final	Decrease (%)	t	p
	$\bar{X} \pm SD$	$\bar{X} \pm SD$			
Vaginal discharge	1.8 $\pm$ 1.1	0.3 $\pm$ 0.5	81.3	7.9	<0.0001*
Odour	0.7 $\pm$ 1.1	0.0 $\pm$ 0.0	100		
Itching	1.0 $\pm$ 1.2	0.0 $\pm$ 0.3	100		
Burning	1.0 $\pm$ 1.2	0.2 $\pm$ 0.5	90	3.9	0.0002*
Vaginal dryness	0.7 $\pm$ 1.2	0.1 $\pm$ 0.3	80	3.1	0.0030*
Total score	5.1 $\pm$ 2.2	0.8 $\pm$ 1.1	84.3	11.1	<0.0001

*Statistically significant at $p < 0.05$.

Table 5. Mean values $\pm$ standard deviations of investigator-assessed signs and symptoms of vulvovaginal disorders at baseline and after treatment with Bioapigyn® pessaries, with corresponding t-test results.

Signs/symptoms	Initial	Final	Decrease (%)	t	p
	$\bar{X} \pm SD$	$\bar{X} \pm SD$			
Oedema	0.3 $\pm$ 0.5	0.0 $\pm$ 0.0	100		
Erythema	0.2 $\pm$ 0.4	0.0 $\pm$ 0.0	100		
Excoriation	0.0 $\pm$ 0.2	0.0 $\pm$ 0.0	100		
Erosion	0.1 $\pm$ 0.3	0.0 $\pm$ 0.0	100		
Vaginal discharge	0.8 $\pm$ 0.5	0.0 $\pm$ 0.0	100		
Total score	1.4 $\pm$ 1.0	0.1 $\pm$ 0.3	92.9	7.9	<0.0001*
Vaginal pH	5.4 $\pm$ 0.8	4.7 $\pm$ 0.6	13.0	4.4	<0.0001*

*Statistically significant at $p < 0.05$.

Among 32 patients with vaginal purity graded as II at baseline based on native wet mount microscopy, normalization to Grade I (normal vaginal flora) was achieved in 28 patients following treatment. In the remaining four patients, the degree of vaginal purity remained unchanged. Following treatment, clinical cure was achieved in 33 of 40 patients (82.5%), while clinical improvement was observed in the remaining 7 participants (17.5%). No patients reported new symptoms or worsening of existing symptoms. On the contrary, all participants reported a reduction in all signs and symptoms of vulvovaginal disorders compared to baseline.

3.3. Comparative efficacy of Acidosalus® and Bioapigyn® pessaries

Direct comparison of the two treatment groups demonstrated comparable clinical efficacy and safety (Figures 1, 2). Both devices achieved symptom reductions exceeding 80%, clinically relevant decreases in vaginal pH, high rates of vaginal flora normalization, and a 100% overall response rate defined as clinical cure or improvement. With the exception of itching, where Bioapigyn® pessaries performed significantly better ($p = 0.0217$), no statistically significant differences were observed for any other sign or symptom between the two medical devices, indicating equivalent clinical performance. The results of this study demonstrate that reformulated

Acidosalus® vaginal pessaries are clinically effective and safe in alleviating symptoms of vulvovaginal disorders associated with elevated vaginal pH. The observed reductions in symptom severity exceeding 80%, together with normalization of vaginal pH and vaginal microflora in the majority of patients, are consistent with the intended physical mode of action of the device.

Restoration of the acidic vaginal environment is a key factor in maintaining vaginal health, as numerous studies have shown a strong association between elevated vaginal pH and the development of bacterial vaginosis and other vulvovaginal disorders (Larsen et al., 2001; Boskey et al., 1999; Klebanoff et al., 1991; Sobel, 2000; Ravel et al., 2011). Disruption of the vaginal microbiota, particularly the

depletion of Lactobacillus-dominated flora, has been identified as a central factor in the pathogenesis and recurrence of these conditions (Ravel et al., 2011; Petrova et al., 2015).

Unlike pharmacological treatments that primarily target specific pathogens, medical devices acting through physical and physicochemical mechanisms support mucosal recovery and stabilization of the vaginal microenvironment, which may contribute to sustained symptom relief and reduced recurrence. This approach is increasingly recognized as a valuable strategy in the management of recurrent or nonspecific vulvovaginal disorders, where restoration of physiological conditions rather than eradication of individual pathogens is essential (Sobel, 2000; Mendling et al., 2019).

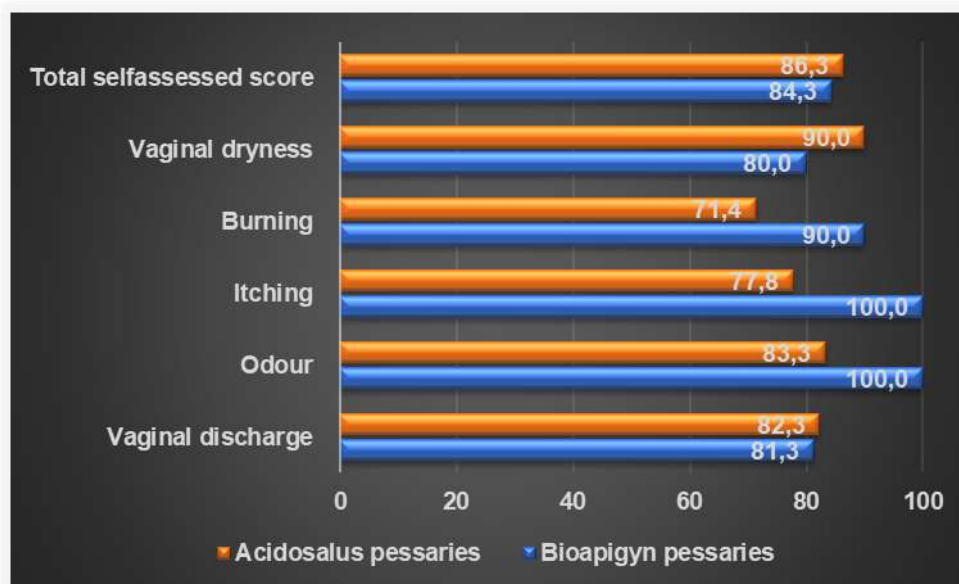


Figure 1. Mean percentage reduction of patient-reported signs and symptoms of vulvovaginal disorders following treatment with Acidosalus® pessaries and the comparator medical device, Bioapigyn® pessaries.

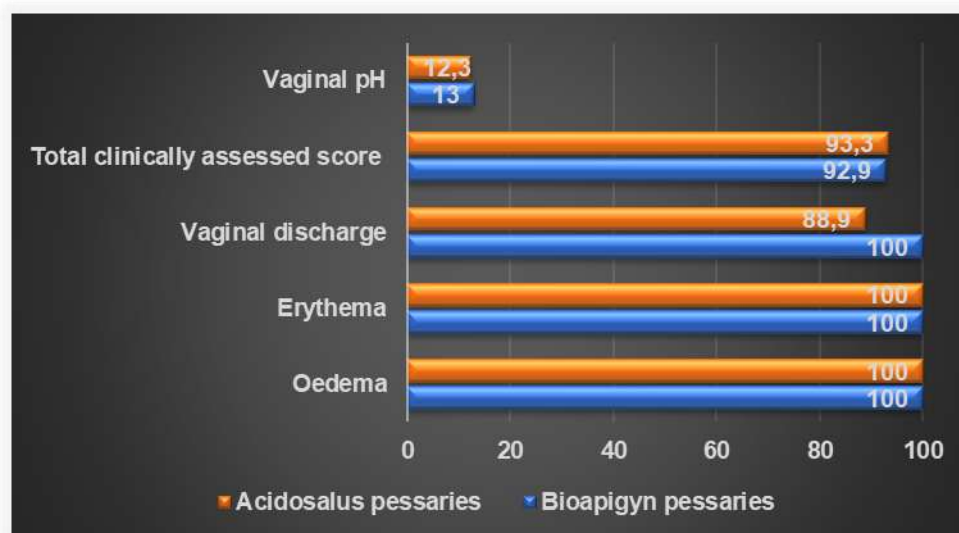


Figure 2. Mean percentage reduction of investigator-assessed signs and symptoms of vulvovaginal disorders following treatment with Bioapigyn® pessaries (comparator medical device) and Acidosalus® pessaries (investigational medical device).

3.5. Safety and tolerability

Safety assessment revealed an excellent tolerability profile for both medical devices. No adverse events, local irritation, allergic reactions, worsening of baseline symptoms, or occurrence of new symptoms were reported in either treatment group. Importantly, no deterioration of vaginal pH or vaginal purity was observed during or after treatment. These findings indicate that both devices are safe for local vaginal use within the prescribed treatment duration.

3.6. Comparison of reformulated and previous Acidosalus® formulations

Safety assessment demonstrated an excellent tolerability profile for both medical devices. No adverse events, local irritation, allergic reactions, worsening of baseline symptoms, or emergence of new symptoms were reported in either treatment group. Importantly, no deterioration in vaginal pH or vaginal purity was observed during or after treatment. These findings indicate that

both devices are safe for local vaginal use within the prescribed treatment duration.

4. Conclusions

The results of this prospective, randomized comparative clinical study demonstrate that reformulated Acidosalus® vaginal pessaries are clinically effective and safe in the treatment of vulvovaginal disorders associated with increased vaginal pH. Treatment resulted in a marked reduction of all key symptoms, clinically relevant restoration of vaginal pH toward the physiological acidic range, and normalization of vaginal microflora in the majority of patients. Overall clinical response was achieved in 100% of treated patients, with 85% clinical cure, 15% clinical improvement, and no clinical failures. Direct comparison with Bioapigyn® vaginal pessaries, an established medical device used for the same indications, showed comparable efficacy and safety profiles, with no clinically meaningful differences in

treatment outcomes between the two products. Both devices were well tolerated, and no adverse events, symptom worsening, or new safety concerns were observed.

Importantly, when contextualized with previously published clinical data on the earlier formulation of Acidosalus® vaginal pessaries, the present results confirm preservation of clinical performance despite reformulation and replacement of live probiotic bacteria with a non-viable probiotic yeast. This demonstrates continuity of clinical benefit across product generations and supports the robustness of the device's physical mode of action. Taken together, these findings provide solid clinical evidence that reformulated Acidosalus® vaginal pessaries meet current requirements of Regulation (EU) 2017/745 and represent a safe and effective non-pharmacological option for the management of vulvovaginal disorders associated with elevated vaginal pH. A limitation of the present study is the relatively small sample size, which may limit the generalizability of the findings. However, this limitation is inherent to premarket clinical investigations of medical devices and will be addressed through ongoing post-market clinical follow-up (PMCF), enabling continuous evaluation of safety and performance throughout the product lifecycle.

Authors Contribution

Višnja Oreščanin: study design, study monitoring, data analysis, manuscript drafting. Rosa Ferinčević: study design, final manuscript review. Štefica Findri Guštek: performing clinical investigations. Marina Ferinčević: study design, final manuscript review.

Conflict of Interest

There is no conflict of interest.

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