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Intravaginal *Aloe barbadensis* and cervical HPV clearance: A retrospective observational study

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Abstract: **Background**: Persistent infection with human papillomavirus (HPV) is a key factor in cervical carcinogenesis. Immune-mediated mechanisms play a central role in viral clearance, leading to interest in immunomodulatory supportive therapies. **Objectives**: This study aimed to evaluate the association between intravaginal *Aloe barbadensis* use and HPV clearance in HPV-positive women. **Methods**: This retrospective observational study included 251 HPV-positive women aged ≥30 years. Of these, 164 received intravaginal *Aloe barbadensis*–containing vaginal capsules for 10 days, while 87 received no immunomodulatory treatment. HPV-PCR and cytological results were evaluated at baseline and after one year of follow-up. **Results**: HPV clearance was observed in 45.7% of patients in the *Aloe barbadensis* group and 36.8% in the control group, with no statistically significant difference between groups ($p = 0.219$). Subgroup analyses based on smoking status and HPV genotype also revealed no significant differences in clearance rates. **Conclusion**: Intravaginal *Aloe barbadensis* use was not associated with a statistically significant improvement in HPV clearance. The findings highlight the complexity of HPV persistence and suggest that single-agent immunomodulatory interventions may have limited clinical impact.

Keywords: *Aloe barbadensis*; Cervical premalign lesion; Clearance; HPV; Immunomodulator

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INTRODUCTION

Cervical cancer is one of the most common gynecological malignancies worldwide and is largely preventable. The primary etiological factor in the development of cervical intraepithelial neoplasia and invasive cervical cancer is persistent human papillomavirus (HPV) infection, particularly with high-risk oncogenic genotypes. However, the persistence of HPV infection and disease progression depend not only on viral characteristics but also on the host's immune response and the local tissue microenvironment. HPV exhibits significant epithelial tropism and has developed various mechanisms to evade host immune surveillance (Ahluwalia *et al*., 2016). These include limiting antigen presentation, suppressing the local cellular immune response and reducing T-cell activity in infected epithelial tissue. These immune evasion strategies contribute to viral persistence, increasing the risk of neoplastic transformation. Therefore, effective HPV clearance largely depends on the integrity of the cellular immune response and the maintenance of local immune regulation (Boudreau and Beland, 2006). In this context, immunity-based treatment approaches for HPV have been developed. Immunomodulatory strategies, such as therapeutic HPV vaccines, aim to strengthen virus-specific cellular immunity. Although these approaches have shown promising results, the variability in clinical responses highlights the complexity of immune control in HPV-related diseases and the limitations of single-target interventions (Cassileth, 2011). These compounds can serve as supportive agents in various plant immune mechanisms, and their potential immunomodulatory and supportive biological effects are under investigation. In this context, *Aloe barbadensis* has been studied in various experimental settings. In this context, *Aloe barbadensis* has primarily been studied *in vitro*. Experiments at the cellular and molecular levels have shown that Aloe barbadensis extracts can affect T-cell activity and modulate the immune response; however, these effects have been reported to be highly dependent on formulation, dose, and experimental conditions (Egawa *et al*., 2015). Following *in vitro* findings, in vivo experimental studies and animal models have been used to evaluate the biological effects of *Aloe barbadensis*. Animal studies have reported that *Aloe barbadensis* can exert biological effects on reproductive tissues and cellular structures, suggesting that these effects are not limited solely to topical wound healing (Gao *et al*., 2019). However, the vast majority of these studies do not include HPV-specific infection models and it is not possible to directly correlate the observed effects with HPV persistence or clearance. *Aloe-emodin*, one of the biologically active components of *Aloe barbadensis*, can exhibit antiproliferative and pro-apoptotic effects in cancer cell models via p53 and p21-mediated pathways (Kaur and Bains, 2024). Furthermore, experimental findings suggest that Aloe-emodin may influence HPV-related oncogenic mechanisms, particularly through E6/E7 oncoprotein activity and cellular metabolism (Kosif and Aktas, 2009). However, these data are largely based on *in vitro* models. In addition to the limited scope of available clinical data, comprehensive evaluations of *Aloe barbadensis* have demonstrated considerable heterogeneity in its biological and toxicological effects. The immunological,

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antiproliferative, and safety profiles of *Aloe barbadensis*–derived products vary substantially depending on dose, exposure duration, route of administration, and pharmaceutical formulation. These variations raise important concerns regarding reproducibility, safety, and clinical applicability, particularly in the context of chronic or intravaginal use. Consequently, translating experimental findings into consistent clinical benefit remains challenging, underscoring the need for well-designed clinical studies that specifically address HPV-related outcomes. Established clinical immunomodulators used in HPV-related diseases, such as topical imiquimod and therapeutic HPV vaccines, target HPV-specific cellular immune responses, have well-defined mechanisms of action, and have been demonstrated to be clinically efficacious in controlled studies. Imiquimod, primarily as a Toll-like receptor 7 (TLR7) agonist, activates innate immune pathways in antigen-presenting cells; it supports a Th1-predominant cellular immune response by increasing type I interferon production (Kuo *et al*., 2002). Therapeutic HPV vaccines, on the other hand, aim to induce antigen-specific $CD8^+$ cytotoxic T cell and $CD4^+$ helper T cell responses by targeting E6 and E7 oncoproteins, which play a critical role in HPV persistence (Psomiadou *et al*., 2020). In contrast, topical products used to relieve vaginal symptoms primarily act by supporting the mucosal barrier, moisturizing, maintaining pH balance, and reducing local irritation, and do not target immunological mechanisms such as activating HPV-specific cellular immunity or directly inducing viral clearance. Aloe barbadensis is considered to occupy an intermediate position between these two approaches. Experimental studies have reported that Aloe barbadensis extracts can modulate T cell activity, affect cytokine production and exhibit regulatory effects on the immune response (Qiu *et al*., 2000). However, these reported effects vary with experimental conditions, preparation content and dose and do not provide a standardized, clinically validated immune effect profile specific to HPV, as is the case with imiquimod or therapeutic HPV vaccines. Therefore, it is not possible to consider the potential immunomodulatory effects of Aloe barbadensis to be directly equivalent to established HPV immunotherapies, and the current data suggest that this plant should be considered more of a supportive or complementary agent.

The aim of this study is to evaluate the association between intravaginal *Aloe barbadensis* use and HPV clearance in HPV-positive women using clinical data, given that HPV persistence is closely related to immune responses, and to investigate whether this relationship can be considered in a supportive context for established HPV immunomodulatory approaches.

MATERIALS AND METHODS

Patients who presented to the Obstetrics and Gynecology Clinic of Selçuk University Faculty of Medicine between 01.012022 and 30.12.2024 with HPV positivity were retrospectively evaluated in an observational, non-randomized design. Patients aged 30 years and older who tested positive for HPV by HPV-PCR and whose smear and HPV-PCR results were available at baseline and at 1 year of follow-up were included in the study. 87 patients did not receive treatment with *Aloe barbadensis* preparations, while 164 did. HPV clearance rates were evaluated at the end of one year of follow-up. Demographic data for patients, including age, gravida, parity, additional diseases, previous operations, HPV types, and smoking history, were obtained from their files. In the outpatient clinic, supportive treatments are provided in accordance with current literature, in collaboration with the patient and physician, in a manner that benefits the patient. The initial diagnosis was based on HPV positivity. This decision was based on the patient's verbal statement that the supportive treatment was used correctly and regularly. A total of 251 patients were included in the study. 164 patients (65.3%) received *Aloe barbadensis* treatment, while 87 patients (34.7%) formed the control group.

Inclusion criteria

Patients who tested positive for HPV via HPV-PCR, were 30 years of age or older, had regular follow-up data, adhered to the recommended treatment protocol throughout the study, and had complete baseline and follow-up results were included in the study.

Exclusion criteria

Patients with a history of partner change, those diagnosed with an additional malignancy during the study, those receiving a different immunomodulatory treatment during follow-up, and those with incomplete clinical data were excluded from the study. The group that underwent conization was not included. Patients with a history of HPV vaccination and those reporting consistent use of condoms or other barrier methods during the follow-up period were excluded from the study.

As an immunomodulator, patients were given intravaginal *Aloe barbadensis* for 10 days (Asos Pharma Vagisimplex-10 capsules). The 10-day intravaginal application regimen was selected based on routine clinical practice and manufacturer usage recommendations rather than on a predefined dose–response hypothesis. Therefore, the duration was intended to reflect real-world clinical use. Vagi-simplex vaginal capsules contain titanium dioxide microcrystals covalently bound to silver ions, sodium hyaluronate, *Aloe barbadensis* extract, caprylic/capric triglycerides, PEG-6 stearate (and) glycol stearate (and) PEG-32 stearate and glyceryl stearate. This composition is thought to support epithelial healing by creating a barrier mechanism. This preparation contains titanium dioxide microcrystals covalently bound to silver ions, known for their antimicrobial properties; sodium hyaluronate, which supports mucosal hydration and epithelial integrity; *Aloe*

barbadensis extract, reported to have biological and potential immunomodulatory effects; caprylic/capric triglycerides, which enhance the stability and adhesion of the formulation to the mucosa; and various emulsifier components (PEG-6 stearate, glycol stearate, PEG-32 stearate and glyceryl stearate). The primary mechanism of action of the preparation is thought to be the creation of a protective barrier in the vaginal mucosa, supporting epithelial healing. Therefore, the clinical effects obtained should be considered to reflect the combined effect of the multi-component structure and barrier-supporting mechanism of the preparation, rather than the immunomodulatory properties of *Aloe barbadensis* alone. Therefore, the potential contribution of *Aloe barbadensis* to HPV clearance was evaluated within the context of this preparation, and the effect could not be interpreted as exclusive to this component.

Statistics

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) 26.0. The suitability of the numerical variables of the patients for normal distribution was determined by examining skewness and kurtosis values. It was observed that age, follow-up period, parity, and the number of children followed a normal distribution. The reference value for the normal distribution is ±1.96 (Kalaycı, 2005). The Chi-Square test was used to compare the age and comorbidity distributions of female patients using Aloe barbadensis according to smoking status, and the Independent Sample T Test was used to compare age, follow-up period, parity, and number of children. Chi-Square test was used to compare the HPV test results before and after using *Aloe barbadensis* cream according to the smoking status of female patients. In the entire study, significance levels were determined using the values 0.05 and 0.01.

RESULTS

The mean age was 47.3±2.3 years and most cases were multiparous. The most common comorbidities were thyroid disorders and diabetes mellitus. No statistically significant differences were observed between the groups in terms of demographic characteristics.

Non-smoking patients who were initially HPV positive were evaluated for HPV types according to their *Aloe barbadensis* use status. In the control group (not using *Aloe barbadensis*), HPV negativity was observed in 11 out of 28 cases (39.3%) infected with other HPV types, while HPV persistence was detected in 17 cases (60.7%); HPV negativity was observed in 4 out of 8 cases (50.0%) positive for HPV 16 and persistence was observed in 4 cases (50.0%); HPV negativity was observed in 2 out of 7 cases (28.6%) positive for HPV 18 and HPV persistence was observed in 5 cases (71.4%). In the group using *Aloe barbadensis*, HPV negativity was observed in 25 out of 40 cases (62.5%) infected with other HPV types, and HPV persistence was detected in 15 cases (37.5%). Of 32 HPV 16-positive cases, 11 (34.4%) showed HPV negativity, while 21 (65.6%) showed HPV persistence; of 11 HPV 18-positive cases, 3 (27.3%) showed HPV negativity, while 8 (72.7%) showed HPV persistence (Table 1).

Initially HPV-positive cases were compared between *Aloe barbadensis* and control groups. In the *Aloe barbadensis* group, HPV negativity was observed in 75 out of 164 cases (45.7%), while HPV persistence was detected in 89 cases (54.3%). In the control group, HPV negativity was observed in 32 out of 87 initially HPV-positive cases (36.8%), while HPV persistence continued in 55 cases (63.2%). Although the HPV negativity rate was higher and the HPV persistence rate was lower in the *Aloe barbadensis* group, this difference was not statistically significant in the comparison between the groups ($\chi^2 = 1.51$; $p = 0.219$).

Patients who were smokers and initially HPV positive were evaluated for HPV types according to their *Aloe barbadensis* use status. In the control group (not using *Aloe barbadensis),* HPV negativity was observed in 12 out of 29 cases (41.4%) infected with other HPV types, while HPV persistence was detected in 17 (58.6%); HPV negativity was observed in only 2 out of 13 cases (15.4%) positive for HPV 16, while persistence continued in 11 (84.6%); HPV negativity was observed in 1 out of 2 cases (50.0%) positive for HPV 18, while HPV persistence was observed in 1 (50.0%). In the group using *Aloe barbadensis,* HPV negativity was observed in 19 out of 34 cases (55.9%) infected with other HPV types and HPV persistence was detected in 15 (44.1%). Of 32 HPV 16-positive cases, 11 (34.4%) showed HPV negativity, while 21 (65.6%) showed HPV persistence; of 15 HPV 18-positive cases, 6 (40.0%) showed HPV negativity, while 9 (60.0%) showed HPV persistence. In the group using *Aloe barbadensis* among smokers, the rate of HPV negativity, especially in HPV 16 infections, was observed to be higher compared to the control group (Table 2).

In non-smoking patients, the use of *Aloe barbadensis* did not provide a significant clearance advantage, especially in HPV 16 and HPV 18 infections. Still, the negativity rates were higher in other HPV types.

Adjusted analyses, confidence intervals and formal interaction testing were not performed due to the retrospective design and limited sample sizes within subgroups.

DISCUSSION

The present retrospective observational study demonstrates that intravaginal administration of a multi-component vaginal preparation containing *Aloe barbadensis* was not associated with a statistically significant improvement in HPV clearance.

Table 1: Overall HPV clearance according to *aloe barbadensis* use

Group	Total (n)	HPV negative n (%)	HPV positive n (%)	p value
Aloe barbadensis used	164	75 (45.7)	89 (54.3)	
Control (no use)	87	32 (36.8)	55 (63.2)	0.219
Total	251	107 (42.6)	144 (57.4)	

Chi-square test; $p < 0.05$ considered statistically significant.

Table 2: HPV clearance according to smoking status, HPV type and *aloe barbadensis* use

HPV type	*Aloe barbadensis* use	Total (n)	HPV negative n (%)	HPV persistent n (%)
Smokers				
Other HPV types	Yes	34	19 (55.9)	15 (44.1)
	No	29	12 (41.4)	17 (58.6)
HPV 16	Yes	32	11 (34.4)	21 (65.6)
	No	13	2 (15.4)	11 (84.6)
HPV 18	Yes	15	6 (40.0)	9 (60.0)
	No	2	1 (50.0)	1 (50.0)
Total	Yes	81	36 (44.4)	45 (55.6)
	No	44	15 (34.1)	29 (65.9)
Non-Smokers				
Other HPV types	Yes	40	25 (62.5)	15 (37.5)
	No	28	11 (39.3)	17 (60.7)
HPV 16	Yes	32	11 (34.4)	21 (65.6)
	No	8	4 (50.0)	4 (50.0)
HPV 18	Yes	11	3 (27.3)	8 (72.7)
	No	7	2 (28.6)	5 (71.4)
Total	Yes	83	39 (47.0)	44 (53.0)
	No	43	17 (39.5)	26 (60.5)

Although numerically higher HPV negativity rates were observed in the intervention group, these differences did not reach statistical significance. This finding underscores the biological complexity of HPV persistence and clearance and suggests that viral elimination cannot be reliably achieved through a single supportive intervention in isolation. *Aloe barbadensis* has been extensively studied for its antioxidant, anti-inflammatory, antiviral, and immunomodulatory properties, and these effects have been well documented across a broad range of experimental and disease models (Schon *et al*., 2003). However, the majority of this evidence is derived from *in vitro* experiments, animal studies, or clinical contexts unrelated to HPV infection. Translating these biological effects into clinically meaningful outcomes in HPV clearance remains challenging, particularly given the heterogeneity in *Aloe* formulations, dosing regimens, routes of administration, and bioavailability reported across studies. This variability likely contributes to the inconsistency observed between experimental findings and clinical outcomes. Several studies have suggested that chemically modified *Aloe barbadensis* polysaccharides may exert immunoregulatory effects by stimulating macrophage activity, fibroblast proliferation, and cytokine production. Importantly, these effects are often observed under experimental conditions using modified compounds or concentrations that may not be achievable in routine clinical practice. In contrast, natural *Aloe* extracts and commercially available multi-component formulations may exhibit substantially weaker or context-dependent immune effects. This distinction highlights the importance of formulation-specific considerations when interpreting clinical efficacy and may partly explain the lack of observed benefit in HPV clearance in the present study. In addition to variability in immunomodulatory potential, the biological activity of *Aloe barbadensis* must be considered alongside its toxicological profile. *Aloe* preparations contain a wide spectrum of biologically active constituents, including vitamins, minerals, polysaccharides, phenolic compounds, and anthraquinone derivatives (Sherer *et al*., 2022). While these components may confer therapeutic potential, there is also evidence that prolonged or high-dose exposure can lead to cytotoxic or genotoxic effects (Silva *et al*., 2023). Consequently, the clinical application of *Aloe-based* products requires careful balancing of potential benefits against safety considerations. In the current study, the dosage and duration of administration were based on manufacturer recommendations rather than on evidence demonstrating optimal biological efficacy for HPV clearance. Although *in-vitro* studies have reported that *Aloe barbadensis* extracts can influence T-cell activity and immune signaling pathways (Talwar *et al*., 2008), the clinical relevance of these findings in the context of active HPV infection remains uncertain. Notably, no immunological endpoints—such as cytokine profiles, T-cell subsets, or mucosal immune markers—were measured

in this study. Consequently, it was not possible to directly assess whether intravaginal *Aloe* administration modulated HPV-specific immune responses *in vivo*. This limitation necessitates cautious interpretation of mechanistic hypotheses and precludes definitive conclusions regarding immune pathways.

HPV clearance is primarily mediated by host cell-mediated immune responses, particularly HPV-specific $CD4^+$ and $CD8^+$ T-cell activity. However, HPV has evolved highly effective immune evasion strategies, including suppression of antigen presentation, downregulation of interferon signaling, and modulation of the local immune microenvironment through the actions of E6 and E7 oncoproteins (Trimble and Frazer, 2009). These mechanisms contribute to viral persistence and limit the effectiveness of non-targeted immunomodulatory interventions. As a result, HPV clearance often requires robust, antigen-specific cellular immune activation rather than generalized immune stimulation. Recent advances in the management of HPV-related disease have increasingly focused on targeted immune-based strategies, including therapeutic HPV vaccines, T-cell–directed immunotherapies, and immune checkpoint inhibitors (Yu et al., 2023). These approaches show variable clinical efficacy depending on HPV genotype, immune status, tumor microenvironment and viral evasion mechanisms. Evidence indicates that effective HPV control usually requires a multimodal approach rather than a single treatment. Therefore, the lack of a significant effect in this study aligns with existing literature and underscores the limited impact of supportive immunomodulators alone. Experimental studies also suggest that Aloe-derived compounds, such as Aloe-emodin, may target HPV oncogenic pathways by modulating E6/E7 expression and inducing apoptosis in cervical cancer cells (Zhu et al., 2025). However, these findings are based solely on in vitro or experimental models and do not directly demonstrate clinical efficacy in HPV clearance. The concentrations used in such studies may not reflect achievable levels with intravaginal application. Additionally, the formulation examined in this study was multi-component, containing not only Aloe barbadensis but also silver ions, sodium hyaluronate and barrier-supporting excipients, each of which may independently affect epithelial healing, antimicrobial activity, or mucosal integrity. Therefore, attributing clinical outcomes to a single component is not methodologically feasible and represents an important confounding factor. Overall, the results do not indicate that Aloe barbadensis is biologically ineffective; rather, intravaginal use of a multi-component Aloe-containing preparation did not achieve clinically meaningful HPV clearance in this retrospective analysis. Given the multifactorial nature of HPV persistence—shaped by viral, immunological, and local tissue factors—standalone immunomodulatory agents should not be expected to produce decisive effects. The lack of statistical significance likely reflects formulation-related limitations, bioavailability issues, and the complex biology of HPV persistence rather than the invalidity of immunomodulation as a concept.

Limitations

Data regarding the use of Aloe barbadensis are based on patient self-reports, and treatment adherence could not be objectively confirmed. The bioavailability of the vaginal formulation used was not compared with other Aloe preparations and immunological markers (cytokines, T cell subgroups, etc.) were not evaluated; this limits interpretations of the mechanism. A one-year follow-up period is insufficient to assess long-term HPV persistence or recurrence. The preparation used in the study was multi-component (Aloe barbadensis extract, silver ions, sodium hyaluronate, and barrier-supporting excipients). Since each component may have independent effects on epithelial healing and the mucosal barrier, it was not possible to isolate the specific effect of Aloe. This is a significant confounding factor limiting causal interpretations. Intravaginal application lasted only 10 days. HPV persistence is a chronic process, and viral clearance usually requires a long-term, robust cellular immune response. Therefore, the limited clinical efficacy may have resulted from the incompatibility of the application duration and dose with the biological nature of HPV. Furthermore, because immunological endpoints were not directly measured, the intervention's potential immunomodulatory effect could not be clearly determined. Therefore, the results should be interpreted cautiously. Future studies with larger sample sizes, prospective and randomized designs, comparisons of different doses, durations, and pharmaceutical forms, and evaluations of immunological and molecular markers are recommended.

CONCLUSION

Intravaginal *administration of Aloe barbadensis* did not demonstrate a significant effect on HPV clearance in this retrospective cohort. The negative findings may be influenced by the multi-component formulation of the intervention, variability in bioavailability, and the absence of immunological endpoint measurements. HPV persistence remains a multifactorial process, and supportive immunomodulatory approaches should be considered complementary rather than definitive therapeutic strategies.

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None.

Authors' contributions

Belma Gözde Özdemir: Study conception and design, data collection, data analysis and interpretation and manuscript drafting; Fazıl Avcı: Data analysis, interpretation of results and critical revision of the manuscript; Leyla Hüseynli: Data collection, literature review and manuscript drafting; Rana Dolaş: Data collection, statistical analysis support and manuscript revision; Ahmet Bilgi: Study design,

supervision and critical revision of the manuscript; Çetin Çelik: Study conception, supervision and final approval of the manuscript. All authors read and approved the final version of the manuscript.

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Data availability statement
The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval
This study was approved by the Selçuk University Ethics Committee (Ethics Committee No: E-70632468-050.01-1103885). This study was performed in adherence with the STROBE guidelines. See supplementary file for the STROBE checklist.

Conflict of interest
The authors declare no conflict of interest.

Artificial intelligence statement
The authors declare that no artificial intelligence (AI)–based tools or technologies were used in writing,

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Consent to publication
The authors confirm that this manuscript is original, has not been published previously in any language or format and is not currently under consideration for publication elsewhere. Written informed consent for publication was obtained from all participants included in the study. The authors retain the signed consent forms and will provide copies to the editors if requested.

Supplementary data
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REFERENCES

Ahluwalia B, Magnusson MK, Isaksson S, Larsson F and Ohman L (2016). Effects of Aloe barbadensis Mill. extract (AVH200®) on human blood T cell activity in-vitro. J. Ethnopharmacol., 179: 301–309.

Boudreau MD and Beland FA (2006). An evaluation of the biological and toxicological properties of Aloe barbadensis (Miller), Aloe vera. J. Environ. Sci. Health C, 24(1): 103–154.

Cassileth B (2011). Aloe vera (*Aloe barbadensis*, *Aloe capensis*). *Oncology (Williston Park)*, **25**(7): 641.

Egawa N, Egawa K, Griffin H and Doorbar J (2015). Human papillomaviruses; epithelial tropisms and the development of neoplasia. *Viruses*, **7**(7): 3863–3890.

Gao R, Wu X, Huang Z, Wang B, Li F, Xu H and Ran L (2019). Anti-tumor effect of Aloe-emodin on cervical cancer cells was associated with human papillomavirus E6/E7 and glucose metabolism. *Onco Targets Ther.*, **12**: 3713–3721.

Kaur S and Bains K (2024). *Aloe barbadensis* Miller (*Aloe vera*). *Int. J. Vitam. Nutr. Res.*, **94**(3-4): 308–321.

Kosif R and Aktas RG (2009). Investigation of the effects of *Aloe barbadensis* on rat ovaries: A preliminary study. *J. Med. Food*, **12**(6): 1393–1397.

Kuo PL, Lin TC and Lin CC (2002). The antiproliferative activity of Aloe-emodin is through p53-dependent and p21-dependent apoptotic pathway in human hepatoma cell lines. *Life Sci.*, **71**: 1879–1892.

Psomiadou V, Iavazzo C, Douligeris A, Fotiou A, Prodromidou A, Blontzos N, Karavioti E and Vorgias G (2020). An alternative treatment for vaginal cuff wart: A case report. *Acta Med. (Hradec Kralove)*, **63**(1): 49–51.

Qiu Z, Jones K, Wylie M, Jia Q and Orndorff S (2000). Modified *Aloe barbadensis* polysaccharide with immunoregulatory activity. *Planta Med.*, **66**(2): 152–156.

Schon MP, Schon M and Klotz KN (2003). The small immune response modifier imiquimod interacts with adenosine receptor signaling pathways to induce cytokine production. *J. Invest. Dermatol.*, **121**(2): 278–284.

Sherer MV, Kotha NV, Williamson C and Mayadev J (2022). Advances in immunotherapy for cervical cancer: Recent developments and future directions. *Int. J. Gynecol. Cancer*, **32**(3): 281–287.

Silva AJD, de Moura IA, da Gama MATM, Leal LRS, de Pinho SS, Espinoza BCF, Santos DLD, Santos VEP, De Sena MGAM, Viana Invencao MDC, de Macêdo LS, de França Neto PL and de Freitas AC (2023). Advancing immunotherapies for HPV-related cancers: Exploring novel vaccine strategies and the influence of tumor microenvironment. *Vaccines (Basel)*, **11**(8): 1354.

Talwar GP, Dar SA, Rai MK, Reddy KV, Mitra D, Kulkarni SV, Doncel GF, Buck CB, Schiller JT, Muralidhar S, Bala M, Agrawal SS, Bansal K and Verma JK (2008). A novel polyherbal microbicide with inhibitory effect on bacterial, fungal and viral genital pathogens. *Int. J. Antimicrob. Agents*, **32**(2): 180–185.

Trimble CL and Frazer IH (2009). Development of therapeutic HPV vaccines. *Lancet Oncol.*, **10**(10): 975–980.

Yu L, Lanqing G, Huang Z, Xin X, Minglin L, Fa-Hui L, Zou H and Min J (2023). T cell immunotherapy for cervical cancer: Challenges and opportunities. *Front. Immunol.*, **14**: 1105265.

Zhu K, Han Y, Zhu Y, Zhu X, Huang S and Wang K (2025). Mechanism of action of *Aloe vera* against human papillomavirus-positive head and neck squamous cell carcinoma. *Oncol. Lett.*, **30**(4): 475.