MINH
MALAHAYATI INTERNATIONAL JOURNAL OF NURSING AND HEALTH SCIENCE
ISSN 2620-9152 (Print)
ISSN 2621-4083 (Online)
DOI: 10.33024
Nomor: 79/E/KPT/2023

ARTICLE INFORMATION
Received: July, 15, 2026
Revised: July, 20, 2026
Available online: August, 24, 2026
at : https://e-jurnal.iphorr.com/index.php/minh

Bladder KI-67 expression and IL-6 levels after *Ipomoea Batatas* extract administration

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Abstract

Background: Estrogen deficiency after menopause contributes to structural and functional alterations of the bladder, including impaired urothelial proliferation, increased oxidative stress, and chronic inflammation. Ki-67 reflects cellular proliferative activity, whereas interleukin-6 (IL-6) represents a key pro-inflammatory mediator involved in tissue injury. *Ipomoea batatas* L., a purple sweet potato rich in anthocyanins and phytoestrogenic compounds, may exert regenerative and anti-inflammatory effects on estrogen-sensitive tissues.
Purpose: To evaluate the effect of *Ipomoea batatas* L. ethanol extract on bladder Ki-67 expression and IL-6 levels in a surgically induced estrogen deficiency (menopause-like) Wistar rat model.
Method: This experimental study used a post-test-only control group design. Thirty-six female Wistar rats were randomly allocated into two groups: a control group receiving distilled water and a treatment group receiving *Ipomoea batatas* L. ethanol extract at 40 mg/kg body weight/day for one month. Menopause was induced through ovariectomy. Bladder tissue samples were collected for assessment of Ki-67 and IL-6 levels. Data normality and homogeneity were assessed using the Shapiro-Wilk and Levene tests, respectively. Between-group comparisons were performed using the independent samples t-test.
Results: The treatment group showed significantly lower IL-6 levels than the control group (14.11 ± 2.45 vs. 28.28 ± 3.58; mean difference 14.17; 95% CI 12.09–16.24; $p < 0.001$). Conversely, Ki-67 expression was significantly higher in the treatment group than in the control group (24.94 ± 3.06 vs. 13.56 ± 2.31; mean difference 11.39; 95% CI 9.55–13.22; $p < 0.001$). Both differences corresponded to very large effect sizes (Cohen's d = 4.62 for IL-6 and 4.20 for Ki-67).
Conclusion: *Ipomoea batatas* L. ethanol extract significantly reduced bladder IL-6 levels and increased Ki-67 expression in menopause-induced Wistar rats. These findings suggest that *Ipomoea batatas* L. may have potential anti-inflammatory and pro-regenerative effects on bladder tissue under estrogen-deficient conditions.

Keywords: Bladder Dysfunction; IL-6; *Ipomoea batatas* L.; Ki-67; Menopause; Phytoestrogen; Wistar rat.

INTRODUCTION

Menopause is a physiological transition characterized by the permanent cessation of menstruation due to the decline of ovarian follicular activity and estrogen production. Although menopause is a natural biological process, estrogen deficiency during the postmenopausal period has important systemic and urogenital consequences. Beyond vasomotor symptoms and metabolic changes, estrogen deprivation affects estrogen-sensitive tissues within the lower urinary tract, including the urethra, bladder trigone, urothelium, and detrusor muscle. These alterations contribute to genitourinary syndrome of menopause and may manifest clinically as urinary frequency, urgency,

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nocturia, recurrent urinary tract infection, overactive bladder, and urinary incontinence (Davis et al., 2015; Robinson, 2024). The increasing number of postmenopausal women worldwide makes lower urinary tract dysfunction an important public health concern, particularly because these symptoms substantially impair quality of life and are often underreported or undertreated (Harlow et al., 2018; Zhang et al., 2024; Christmas et al., 2023).

Estrogen plays a critical role in maintaining the structural integrity and biological function of the lower urinary tract. Estrogen receptors are expressed in urogenital tissues, where estrogen contributes to epithelial maturation, mucosal thickness, periurethral vascularity, collagen metabolism, smooth muscle function, and sensory modulation of bladder activity. Estrogen deficiency may therefore lead to progressive urothelial thinning, impaired tissue repair, reduced blood flow, altered detrusor responsiveness, and increased susceptibility to chronic irritation and inflammation (Robinson & Cardozo, 2003; Hillard, 2010; Robinson, 2024). Experimental and clinical evidence suggests that estrogen depletion is associated not only with anatomical changes but also with molecular disturbances involving proliferative and inflammatory pathways in bladder tissue. These mechanisms provide a biologically plausible link between menopause, bladder remodeling, and lower urinary tract symptoms (Cardozo et al., 2004; Zhang et al., 2024).

Ki-67 is a well-established nuclear protein that is strongly associated with cellular proliferation. It is expressed during the active phases of the cell cycle, including G1, S, G2, and mitosis, but is absent in quiescent cells, making it a reliable marker of proliferative activity in tissue regeneration and pathological remodeling (Scholzen & Gerdes, 2000). In estrogen-sensitive tissues, reduced estrogenic stimulation may impair epithelial turnover and regenerative capacity, whereas estrogenic or estrogen-like compounds may enhance mucosal proliferation through estrogen receptor-mediated pathways. Therefore, Ki-67 expression may serve as a useful biomarker to evaluate the regenerative response of bladder tissue under estrogen-deficient conditions (Nery-Aguiar et al., 2016; Sun & Kaufman, 2018).

In contrast, interleukin-6 (IL-6) represents a key pro-inflammatory cytokine involved in acute and chronic inflammatory responses, immune regulation, tissue injury, and remodeling. Although transient IL-6 production is essential for host defense, persistent IL-6 upregulation may contribute to chronic inflammation and progressive tissue damage (Tanaka et al., 2014; Kang et al., 2019). Estrogen deficiency has been associated with increased oxidative stress and inflammatory activation, which may further aggravate bladder tissue injury in postmenopausal conditions. Accordingly, IL-6 may function as a relevant inflammatory biomarker for assessing the impact of estrogen deprivation and potential therapeutic interventions on bladder inflammation (Tanaka et al., 2014; Kang et al., 2019).

Hormonal therapy remains an effective treatment for several menopausal urogenital symptoms; however, its use may be limited by contraindications, safety concerns, and patient preference. These limitations have encouraged increasing interest in plant-derived compounds with estrogen-like, antioxidant, and anti-inflammatory properties. Phytoestrogens are non-steroidal plant compounds that can interact with estrogen receptors and modulate biological pathways related to oxidative stress, inflammation, and tissue repair (Bedell et al., 2014; Desmawati & Sulastri, 2019). *Ipomoea batatas* L., particularly purple sweet potato, is rich in anthocyanins and other flavonoid compounds with reported antioxidant, anti-inflammatory, and phytoestrogenic activities. Previous studies have shown that purple sweet potato extract may modulate estrogen receptor expression and antioxidant activity in menopause-related animal models, supporting its potential biological relevance in estrogen-deficient conditions (Sugiritama et al., 2020; Silva-Correa et al., 2025).

Emerging experimental data suggest that anthocyanin-rich interventions may have protective effects on bladder remodeling and dysfunction. A blueberry-enriched diet, for instance, was reported to attenuate bladder dysfunction, oxidative stress, and remodeling in a rat model of bladder outlet obstruction (Miyazaki et al., 2020). More specifically, purple sweet potato ethanol extract has been shown to improve urothelial and smooth muscle thickness in

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ovariectomized Wistar rats, suggesting a possible beneficial effect on bladder histomorphology under estrogen-deficient conditions (Putra et al., 2023; Setiawan et al., 2022). Although these earlier studies documented histomorphological changes such as urothelial and smooth-muscle thickening, the specific molecular response of the bladder — in particular, whether the extract can simultaneously dampen local inflammatory signaling and promote epithelial proliferation — has not been directly examined. Evidence regarding the effect of *Ipomoea batatas* L. extract on molecular markers of bladder proliferation and inflammation remains limited. In particular, its influence on Ki-67 expression and IL-6 levels in bladder tissue during menopause-related estrogen deficiency has not been sufficiently clarified. Therefore, this study aimed to evaluate the effect of *Ipomoea batatas* L. ethanol extract on bladder Ki-67 expression and IL-6 levels in a menopause-induced Wistar rat model.

RESEARCH METHOD

An experimental laboratory study using a post-test-only control group design was employed. The study was conducted to evaluate the effect of *Ipomoea batatas* L. ethanol extract on Ki-67 and interleukin-6 (IL-6) levels in bladder tissue from surgically induced estrogen deficiency (menopause-like) female Wistar rats. The animals were randomly allocated into two groups: a control group receiving distilled water and a treatment group receiving *Ipomoea batatas* L. ethanol extract at a dose of 40 mg/kg body weight/day. The primary outcomes were bladder Ki-67 and IL-6 levels measured after completion of the intervention period.

Animal maintenance, daily monitoring, and bladder tissue collection were performed at the Integrated Biomedical Laboratory Unit, Faculty of Medicine, Universitas Udayana, Bali, Indonesia. Preparation of *Ipomoea batatas* L. ethanol extract was conducted at the Pharmacology Laboratory, Faculty of Medicine, University of Udayana. Ki-67 and IL-6 examinations were performed at the Biochemistry and Molecular Biology Laboratory, Faculty of Medicine, University of Udayana.

The study population consisted of female Wistar rats (Rattus norvegicus) aged 2–3 months and weighing 200–300 g. The animals were housed in standardized plastic cages with wire covers and were provided food and water *ad libitum*. Environmental conditions, including lighting, temperature, humidity, cage hygiene, and feeding conditions, were standardized across groups. The room temperature was maintained at approximately 25°C to minimize stress and environmental variability.

The minimum sample size was calculated using Federer's formula, (t-1) (n-1) ≥ 15, where t represents the number of treatment groups and n represents the number of animals per group. With two experimental groups, the minimum estimated sample size was 16 animals per group. After allowing for an anticipated dropout rate of approximately 10%, the final sample size was increased to 18 rats per group, yielding a total of 36 rats. Eligible animals were selected using random sampling and allocated into the control and treatment groups. Group assignment followed a simple randomization procedure based on a computer-generated random-number sequence, and the allocation list was held by an investigator who was not involved in outcome assessment, so that laboratory personnel remained unaware of group identity until all analyses were complete. Federer's formula was selected for sample-size estimation because it is an established and widely applied method for determining the minimum number of animals per group in experimental designs with a small number of treatment arms, and it is consistent with the 3Rs principle of using the fewest animals necessary to obtain valid results.

Purple sweet potato tubers (*Ipomoea batatas* L.) were obtained from Bukian Village, Payangan District, Gianyar Regency, Bali, Indonesia. A total of 3 kg of tubers was washed thoroughly, sliced thinly, and dried in an oven at 60°C. The dried tubers were ground into powder using a blender. Two kilograms of powdered tuber were macerated with 5 L of 96% ethanol for 72 hours. The macerate was filtered using a Buchner funnel, and the filtrate was evaporated using a rotary vacuum evaporator at 70°C, followed by concentration in a water bath at 60°C until a thick extract was obtained.

The menopause model was induced by bilateral ovariectomy. Rats were anesthetized using ketamine 80 mg/kg and xylazine 10 mg/kg intraperitoneally. A small transverse abdominal incision was made in the mid-abdominal region slightly to the right side to

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expose the abdominal wall and peritoneal cavity. The periovarian fat pad was carefully exteriorized until the uterine tube and ovary were identified. The distal uterine horn was ligated with silk suture, and the ovary was removed. The same procedure was performed on the contralateral ovary through the same incision. The uterine horns were returned to the abdominal cavity, the abdominal muscle and skin were closed, and the wound was cleaned. Postoperative recovery was monitored in a clean cage with warming support, and postoperative analgesia was provided according to laboratory animal care procedures.

After a 7-day recovery period following ovariectomy, the animals were divided into two groups. The control group received 2 mL of distilled water, whereas the treatment group received *Ipomoea batatas* L. ethanol extract at a dose of 40 mg/kg body weight/day (Sugiritama et al.; 2020). Both distilled water and extract were administered orally using an oral gavage tube for 30 consecutive days. At the end of the intervention period, the animals were euthanized under deep ketamine anesthesia followed by exsanguination, and bladder tissue samples were then collected for Ki-67 and IL-6 analysis.

Bladder tissue was collected after anesthesia with ketamine 50 mg/kg intramuscularly. A suprapubic incision was performed to expose and remove the bladder. Tissue samples were rinsed in phosphate-buffered saline and preserved at −20°C before further processing. The bladder tissue was subsequently fixed in 10% phosphate-buffered formalin for 24 hours, dehydrated using graded ethanol concentrations, cleared with xylene, and embedded in paraffin blocks. Tissue sections were cut at 5 µm thickness for biomarker assessment.

Both Ki-67 and IL-6 were assessed in bladder tissue by immunohistochemistry. Paraffin-embedded sections were immunostained using the Dako EnVision+ Dual Link System-HRP (DAB+) with primary antibodies directed against Ki-67 and IL-6, and the antigen–antibody reaction was visualized with 3,3'-diaminobenzidine. Immunostained sections were examined under an Olympus CX41 light microscope, and representative fields were captured using OptilabPro imaging. Ki-67 positivity was defined as distinct brown nuclear staining, whereas IL-6 positivity was defined as brown cytoplasmic staining. For each animal, positively stained cells were counted in five non-overlapping high-power fields, and each biomarker was expressed as the percentage of positive cells relative to the total number of cells counted. All slides were coded prior to assessment and scored by a single observer who was blinded to group allocation.

The independent variable was administration of *Ipomoea batatas* L. ethanol extract at 40 mg/kg body weight/day for 30 days. The dependent variables were Ki-67 and IL-6 levels in bladder tissue, both analyzed as numerical variables. Controlled variables included age, sex, body weight, animal model, food type and quantity, housing conditions, lighting exposure, room temperature, air circulation, and the number of animals in each group.

Data were entered and analyzed using Statistical Package for the Social Sciences version 25. Descriptive statistics were used to summarize the distribution of each variable. The Shapiro-Wilk test was used to assess data normality because each group contained fewer than 50 animals. Homogeneity of variance was evaluated using Levene's test. Between-group comparisons were performed using the independent samples t-test when data were normally distributed and homogeneous. If the assumptions of normality and homogeneity were not met, the Mann-Whitney U test was planned as the non-parametric alternative. Statistical significance was defined as $p < 0.05$.

The study was submitted to the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana/Prof. Dr. I.G.N.G. Ngoerah General Hospital for ethical approval (approval number 2983/UN14.2.2.VII.14/LT/2024). Research permission was also obtained from the Integrated Biomedical Laboratory Unit before study implementation. Animal handling, postoperative monitoring, sacrifice, and tissue management were performed according to laboratory animal care standards.

RESEARCH RESULTS

A total of 36 menopause-induced female Wistar rats were included in the final analysis, with 18 rats allocated to the control group and 18 rats allocated to the *Ipomoea batatas* L. extract treatment group. The primary outcomes were bladder IL-6 levels and Ki-67 expression after completion of the intervention period.

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The distribution of both outcome variables was normal in each study group. For IL-6 levels, the Shapiro-Wilk test showed normal distribution in the control group (p = 0.623) and treatment group (p = 0.733). Similarly, Ki-67 expression was normally distributed in both the control group (p = 0.968) and treatment group (p = 0.610). Levene's test also demonstrated homogeneity of variance for IL-6 (p = 0.143) and Ki-67 (p = 0.162), supporting the use of independent samples t-test for between-group comparisons.

Bladder IL-6 levels were significantly lower in the treatment group compared with the control group. The mean IL-6 level in the control group was 28.28 ± 3.58, whereas the mean level in the *Ipomoea batatas* L. extract group was 14.11 ± 2.45. The mean difference between groups was 14.17, with a 95% confidence interval of 12.09 to 16.24 and a standard error of 1.02. This difference was statistically significant (p < 0.001).

In contrast, bladder Ki-67 expression was significantly higher in the treatment group than in the control group. The mean Ki-67 expression in the control group was 13.56 ± 2.31, while the mean expression in the *Ipomoea batatas* L. extract group increased to 24.94 ± 3.06. The mean difference between groups was 11.39, with a 95% confidence interval of 9.55 to 13.22 and a standard error of 0.90. This increase was statistically significant (p < 0.001). The magnitude of both effects was very large: the standardized mean difference (Cohen's d) was 4.62 for IL-6 and 4.20 for Ki-67, indicating a substantial separation between the two groups.

Overall, administration of *Ipomoea batatas* L. ethanol extract was associated with a significant reduction in bladder IL-6 levels and a significant increase in Ki-67 expression compared with the control group. These findings indicate that *Ipomoea batatas* L. extract may exert anti-inflammatory and pro-proliferative effects on bladder tissue under estrogen-deficient conditions.

Table 1. Experimental Group Allocation and Intervention Protocol (N=18)

Group	Animal model	Intervention	Dose	Duration	Primary Outcomes
Control	Menopause-induced female Wistar rats	Distilled water	2 mL/day	30 days	Bladder IL-6 and Ki-67
Treatment	Menopause-induced female Wistar rats	*Ipomoea batatas* L. ethanol extract	40 mg/kgBW/day	30 days	Bladder IL-6 and Ki-67

Note: BW: body weight; IL-6: interleukin-6. Total sample size was 36 rats, with 18 rats in each group.

Table 2. Normality and Homogeneity Tests of Bladder IL-6 and Ki-67 Levels

Variable	Group	Mean ± SD	Shapiro-Wilk p-value	Levene's test p-value
IL-6	Control	28.28 ± 3.58	0.623	0.143
IL-6	Treatment	14.11 ± 2.45	0.733	0.143
Ki-67	Control	13.56 ± 2.31	0.968	0.162
Ki-67	Treatment	24.94 ± 3.06	0.610	0.162

Note: Data were normally distributed based on Shapiro-Wilk test and showed homogeneous variance based on Levene's test.

Table 3. Comparison of bladder IL-6 and Ki-67 levels between control and treatment groups

Variable	Control Group, Mean ± SD	Treatment Group, Mean ± SD	Mean Difference	95% CI	Standard Error	p-value
IL-6	28.28 ± 3.58	14.11 ± 2.45	14.17	12.09–16.24	1.02	<0.001
Ki-67	13.56 ± 2.31	24.94 ± 3.06	11.39	9.55–13.22	0.90	<0.001

Note: Between-group comparisons were performed using independent samples t-test. CI: confidence interval; SD: standard deviation.

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DISCUSSION

This study demonstrated that oral administration of *Ipomoea batatas* L. ethanol extract significantly reduced bladder IL-6 levels and increased Ki-67 expression in menopause-induced Wistar rats. These findings suggest that *Ipomoea batatas* L. may exert dual biological effects on estrogen-deficient bladder tissue: attenuation of inflammatory activity and enhancement of cellular proliferative response. The magnitude of the observed differences was substantial, with lower IL-6 levels and higher Ki-67 expression in the treatment group compared with the control group, indicating that the extract may influence key molecular pathways involved in bladder remodeling under hypoestrogenic conditions.

The reduction in IL-6 observed in the treatment group supports the potential anti-inflammatory effect of *Ipomoea batatas* L. in bladder tissue. IL-6 is a central cytokine in inflammatory signaling and is involved in immune activation, acute-phase responses, and chronic tissue injury. Persistent IL-6 activation may contribute to local inflammation and progressive tissue remodeling, particularly in conditions characterized by oxidative stress and hormonal deprivation (Tanaka et al., 2014; Kang et al., 2019). Estrogen deficiency after menopause has been associated with increased oxidative stress and inflammatory activation in estrogen-sensitive tissues, including the lower urinary tract. Therefore, the significant decrease in IL-6 after *Ipomoea batatas* L. administration may reflect suppression of inflammatory signaling in the estrogen-deficient bladder microenvironment.

The increase in Ki-67 expression in the treatment group indicates a possible pro-regenerative or pro-proliferative effect of *Ipomoea batatas* L. extract on bladder tissue. Ki-67 is widely recognized as a marker of cellular proliferation because it is expressed during active phases of the cell cycle and absent in resting cells. Beyond being a proliferation marker, Ki-67 also has functional roles in chromatin organization and mitotic chromosome behavior, making it biologically relevant in tissue turnover and repair (Sun & Kaufman, 2018). In the context of estrogen deficiency, reduced proliferative activity may contribute to urothelial thinning, impaired mucosal integrity, and vulnerability to irritation. The higher Ki-67 expression found in the treatment group may therefore indicate improved cellular turnover within bladder tissue.

These findings are biologically plausible because *Ipomoea batatas* L., particularly purple sweet potato, contains anthocyanins and other flavonoid compounds with antioxidant, anti-inflammatory, and phytoestrogen-like properties. Phytoestrogens may interact with estrogen receptors and partially mimic estrogenic activity, although their potency is generally weaker than endogenous estrogen. In estrogen-sensitive lower urinary tract tissues, estrogen contributes to epithelial maturation, vascularity, connective tissue support, detrusor function, and modulation of bladder sensory activity. Prior reviews have emphasized the role of estrogens in female lower urinary tract physiology and in urogenital atrophy after menopause (Robinson & Cardozo, 2003; Robinson, 2024).

Thus, the observed changes in Ki-67 and IL-6 may be partly mediated by estrogen receptor-related pathways, antioxidant activity, or both; however, because estrogen-receptor expression and oxidative-stress markers were not measured in the present study, these mechanisms remain hypothetical and cannot be confirmed from the current data.

The present results are consistent with earlier experimental evidence suggesting that anthocyanin-rich interventions may protect bladder tissue from oxidative stress and remodeling. Miyazaki et al. reported that blueberry intake attenuated bladder dysfunction in bladder outlet obstruction rats by reducing oxidative stress and suppressing bladder remodeling, including fibrosis and connexin-43 expression (Miyazaki et al., 2020). Although the pathological model used in that study differs from menopause-induced estrogen deficiency, both conditions share inflammatory and oxidative mechanisms that may contribute to bladder dysfunction. This supports the broader hypothesis that anthocyanin-rich botanical compounds may modulate bladder tissue injury through antioxidant and anti-inflammatory pathways.

The findings also align with previous research on purple sweet potato extract in menopause-related experimental models. Prior work has shown that *Ipomoea batatas* L. ethanol extract improved urothelial and smooth muscle thickness in ovariectomized Wistar rats, suggesting a favorable histomorphological effect on bladder tissue under

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estrogen-deficient conditions. The current study extends that evidence by showing changes in molecular biomarkers, namely increased Ki-67 and reduced IL-6. This is important because structural improvement alone does not fully explain whether the tissue response is related to enhanced regeneration, reduced inflammation, or both. By evaluating both a proliferative marker and an inflammatory cytokine, this study provides a more detailed biomarker-level characterization of the potential bladder-protective effects of *Ipomoea batatas* L.

From a translational perspective, these findings suggest that *Ipomoea batatas* L. may have potential as a complementary botanical candidate for further investigation in menopause-associated bladder dysfunction. However, the findings should not be interpreted as direct clinical evidence, as this study was conducted in an ovariectomized rat model and assessed tissue biomarkers rather than functional urodynamic parameters or clinical symptoms. Thus, although the results support a plausible biological effect, they remain preclinical. Further functional and clinical studies are needed before these findings can be translated into clinical recommendations for postmenopausal women.

Several limitations should be acknowledged. First, this study used only one dose of *Ipomoea batatas* L. extract, preventing evaluation of a dose-response relationship. Second, the study assessed outcomes after a single intervention duration, so the long-term effects and safety profile remain unclear. Third, although Ki-67 and IL-6 are relevant biomarkers, they do not fully represent the complexity of bladder dysfunction. Additional markers related to oxidative stress, apoptosis, estrogen receptor signaling, fibrosis, angiogenesis, and urothelial barrier integrity would strengthen mechanistic interpretation. Fourth, functional outcomes such as bladder capacity, voiding frequency, detrusor contractility, or cystometric parameters were not assessed. Finally, the study did not include a positive control group receiving estrogen therapy, which would have helped determine whether the observed effect of *Ipomoea batatas* L. resembles or differs from conventional estrogenic stimulation. In addition, the success of the ovariectomy-induced estrogen-deficient state was not confirmed biochemically (for example, by measuring serum estradiol or follicle-stimulating hormone) or by vaginal cytology, so the depth of estrogen deprivation could not be quantified. Finally, the ethanol extract was not phytochemically standardized; its total anthocyanin, flavonoid, and phenolic content was not quantified and the extraction yield was not reported, which limits precise reproducibility of the dosing.

Future studies should evaluate multiple doses and treatment durations, include estrogen-treated positive controls, and incorporate both molecular and functional endpoints. Assessment of estrogen receptor α and β expression, oxidative stress markers such as malondialdehyde or 8-hydroxy-2'-deoxyguanosine, antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, and histological parameters such as urothelial thickness, smooth muscle thickness, and collagen deposition would provide a more comprehensive mechanistic framework. Functional bladder evaluation using cystometry would also be important to determine whether biomarker changes translate into meaningful improvement in bladder function.

In conclusion, *Ipomoea batatas* L. ethanol extract significantly decreased bladder IL-6 levels and increased Ki-67 expression in menopause-induced Wistar rats. These findings suggest that the extract may attenuate inflammatory activity and enhance proliferative repair in estrogen-deficient bladder tissue. Although further mechanistic and functional studies are required, this study provides preliminary experimental evidence supporting the potential role of *Ipomoea batatas* L. as a phytoestrogen-rich botanical candidate for further research in menopause-associated bladder dysfunction.

CONCLUSION

In this menopause-induced Wistar rat model, oral administration of *Ipomoea batatas* L. ethanol extract significantly reduced bladder IL-6 levels and increased Ki-67 expression compared with the control group. These findings indicate that *Ipomoea batatas* L. may exert anti-inflammatory and pro-regenerative effects on bladder tissue under estrogen-deficient conditions. Although promising, these results remain preclinical and should be further validated through dose-response studies, functional bladder assessments, and mechanistic evaluation of estrogen receptor, oxidative stress, and tissue-remodeling pathways before clinical translation.

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DECLARATIONS

Ethics approval and animal welfare

This experimental animal study was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia. All animal procedures, including ovariectomy, postoperative monitoring, oral intervention, sacrifice, and bladder tissue collection, were conducted in accordance with institutional laboratory animal care standards. The study used menopause-induced female Wistar rats, which were allocated into a control group receiving distilled water and a treatment group receiving *Ipomoea batatas* L. ethanol extract at 40 mg/kg body weight for 30 days.

Consent to participate

Not applicable. This study did not involve human participants.

Consent for publication

Not applicable. This manuscript does not contain individual human data, images, or identifiable personal information.

Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contributions

NP conceptualized the study, designed the experimental protocol, conducted the animal intervention, collected bladder tissue samples, analyzed the data, interpreted the findings, and drafted the manuscript. KBS supervised the study design, methodology, data interpretation, and manuscript revision. KPY provided scientific input, critical review, and approval of the final manuscript. All authors read and approved the final version of the manuscript.

Acknowledgements

The authors would like to thank the Department of Surgery, Faculty of Medicine, Universitas Udayana, and Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia, for their academic and institutional support. The authors also acknowledge the Integrated Biomedical Laboratory Unit, the Pharmacology Laboratory, and the Biochemistry and Molecular Biology Laboratory, Faculty of Medicine, Universitas Udayana, for their assistance in animal maintenance, extract preparation, and biomarker assessment.

Reporting guideline

This animal experimental study was prepared in accordance with the principles of transparent reporting for preclinical animal research. This study was reported in accordance with the ARRIVE 2.0 guidelines. Housing and husbandry conditions, humane endpoints, and criteria for animal exclusion were pre-specified; all 36 randomized animals completed the study and were included in the analysis, and no unexpected adverse events or mortality occurred. A completed ARRIVE checklist is available and can be submitted alongside the manuscript.

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DOI: https://doi.org/10.33024/minh.v9i6.3917

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