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Effects of *Cassia alata Linn* on bowel function recovery following surgery for gynecological cancer: A randomized controlled trial

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ABSTRACT

Background: Postoperative ileus is a common complication following abdominal surgery. This study was undertaken to determine the effectiveness and safety of *Cassia alata Linn* in stimulating gastrointestinal function recovery among women with gynecologic cancer who had undergone laparotomy for surgical staging or cytoreductive surgery.

Methods: A total of 90 participants were randomly allocated to postoperative consumption of either *Cassia alata Linn* tea (n = 45) or warm water (N = 45). Outcomes of interest included time to first passage of flatus, time to first defecation, time to toleration of solid food, and ileus symptoms. Differences between the groups were measured as mean difference (MD) or odds ratio (OR) with 95% confidence interval (CI).

Results: Women allocated to the *Cassia alata Linn* group had shorter times to first passage of flatus (MD −8.53; 95% CI −3.69, −13.38 h) and first defecation (MD −19.83; 95% CI −11.18, −28.48 h) compared with controls. There were no differences in terms of time to toleration of solid food (MD 0.26; 95% CI −2.13, 1.61 h) or ileus symptoms (OR 0.10; 95% CI 0.01, 1.94) between the two groups.

Conclusion: Postoperative consumption of *Cassia alata Linn* hastens gastrointestinal function recovery after laparotomy in women with gynecologic cancer.

1. Introduction

Postoperative ileus (POI), transient impairment of coordinated gastrointestinal motility secondary to surgical trauma, is a common complication following major abdominal surgery.[1] Ileus predisposes patients to gastrointestinal tract obstruction, prolongs the length of hospital stay, and increases hospital costs.[1–3] Common symptoms of POI include failure to pass flatus or stool, nausea, vomiting, and abdominal pain.[1,2] Women with gynecologic cancer who undergo abdominal surgery for surgical staging of cancer or cytoreductive surgery are at high risk for developing POI because of the complexity of these operations.[4] The incidence of POI after major surgery for gynecologic cancer varies from 10% to 50%.[5,6] Effective intervention to hasten the recovery of gastrointestinal function following extensive surgery for gynecologic cancer is therefore of the utmost importance.

Cassia alata Linn (also known as *Senna alata*) is a plant commonly used for medicinal purposes.[7] The active chemical constituents of *Cassia alata Linn* are phenolics, fatty acids, terpenoids, and anthraquinones.[7–8] Anthraquinone is an active compound in *Cassia alata Linn* that exhibits a laxative effect by stimulating bowel movement.[8] A previous randomized controlled trial found that the consumption of *Cassia alata Linn* infusion was able to more effectively alleviate constipation than a placebo, without any serious adverse events.[9] This suggests that *Cassia alata Linn* might promote the recovery of gastrointestinal function after abdominal surgery. This randomized controlled trial was accordingly undertaken to determine the safety and effectiveness of *Cassia alata Linn* for alleviating POI. We examined women with gynecologic cancer who had undergone laparotomy for surgical staging or cytoreductive surgery, a group of patients likely to experience delayed recovery of gastrointestinal function after surgery.

2. Methods

2.1. Setting and population

This randomized controlled trial was undertaken at Khon Kaen University's Srinagarind Hospital between September 2018 and May 2019. Participants were women 18–70 years of age with clinical

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diagnoses of gynecologic cancer who planned to undergo laparotomy for tumor staging or cytoreductive surgery. Exclusion criteria were a history of inflammatory bowel disease, a history of bowel surgery, current diarrhea, symptoms or signs of gastrointestinal obstruction, abdominal pain with unknown cause, pregnancy, and lactation. Participants were withdrawn from the analysis when they required admission to the intensive care unit or there was a need for nasogastric tube drainage beyond the first postoperative morning. Ethical oversight was provided by the Khon Kaen University Ethics Committee for Human Research (HE611182). Written informed consent was obtained from all participants. This trial was performed and reported in compliance with the CONSORT statement[10] and was registered with the Thai Clinical Trial Register (TCTR0180828004).

2.2. Sample size calculation

The mean ± standard deviation of the time to first passage of flatus in women allocated to the control group was 41.6 ± 10.9 h. This was based on a study by Güngördük et al.,[11] which was conducted to assess the effects of coffee on the recovery of gastrointestinal function after surgery among women with gynecologic cancer. We hypothesized that the time to the first passage of flatus would be reduced by at least 8 h in the *Cassia alata Linn* group. Based on a power of 90%, a type I error of 0.05, and a predicted withdrawal rate of 10%, the sample size needed for testing our primary outcome was 90 women, with 45 in each group.

2.3. Randomization and intervention

When participants were admitted to the hospital, they were randomly allocated to one of the comparison groups using computer-generated block randomization of varying block size. The assigned treatment was noted on cards, which were sealed in secure opaque envelopes. The envelopes were then numbered in sequence and kept and opened by an independent researcher in an office outside of the hospital. Although the surgeon, anesthesiologists, and investigator assessing outcomes were blinded to the intervention allocated, we were unable to blind the participants because of the nature of the study.

On the morning after surgery, participants allocated to the intervention group drank 120 ml of *Cassia alata Linn* infusion prepared by boiling 3 g of *Cassia alata Linn* in water for 10–15 min. Patients were asked to drink the entire amount within 15 min under the supervision of a nurse or doctor. The *Cassia alata Linn* used in this study was prepared and distributed by Chaophraya Abhaibhubejhr Hospital (Thailand). Pricing for 3 g of *Cassia alata Linn* is 7 Thai Baht. Participants allocated to the control group drank 120 ml of warm water instead.

All subjects received the same postoperative care protocol. The use of pelvic drain was at the surgeon's discretion. Generally, surgical drains were solely used after complicated procedures and were removed as early as possible. Histamine H2 blockers were intravenously administered to all participants in the first 24 h following the operation to prevent stress-induced gastritis. Early ambulation was initiated on the morning after surgery. The patients were put on a liquid diet on the first postoperative day and progressed to a solid diet within 24 h, if feasible. To minimize the effects of other variables, postoperative gum-chewing and consumption of either caffeinated or decaffeinated beverages were not allowed.

The hospital discharge was made based on the decision of the staff in charge. In general, the criteria for hospital discharge consisted of stable vital signs with no febrile morbidity for ≥ 48 h, the passage of stool, toleration of a solid diet, and the absence of other postoperative complications.

2.4. Outcomes and measurements

The primary outcome was the time to the first passage of flatus after surgery. The secondary outcomes included the time to the first defecation, number of audible bowel movements at 12 and 24 h after operation, time to toleration of solid food, severe ileus symptoms, adverse events, and length of hospital stay. Time to first flatus was defined as time elapsed between the end of surgery (defined as when the patients regained consciousness) until the first flatus reported by the patients. Time to first defecation was defined as time elapsed between the end of surgery until the first defecation reported by the patients. Time to tolerance of solid food was measured from the end of surgery until the patient was able to tolerate the intake of solid food (any food that required chewing) without nausea or vomiting within 4 h after consumption. A patient was considered to have severe ileus symptoms when additional treatment was required. Participants were instructed to notify ward nurses or investigators immediately after the first occurrence of flatus or defecation so that recovery of bowel function could be measured precisely.

2.5. Statistical analyses

Statistical analyses were performed using Stata 10 (Stata Corporation, College Station, Texas). Descriptive statistics were used to report participants' baseline characteristics. Differences between the comparison groups were measured as mean difference (MD) or odds ratio (OR) with their associated 95% confidence interval (CI). Firth's logistic regression, an approach for analyzing binary outcomes in small sample sizes or rare events, was used to calculate OR. All analyses were carried out based on the intention-to-treat principle.

3. Results

Of the 108 women who were assessed for eligibility, 90 met the inclusion criteria and were randomly allocated to either the *Cassia alata Linn* group (n = 45) or the control group (N = 45). Fig. 1 shows the CONSORT flow diagram of this study. No participants withdrew after the assignment of the intervention.

Table 1 displays participants' baseline characteristics and operative findings stratified by the intervention allocated. The mean age of participants was 54.6 years. Ovarian cancer was the most common preoperative diagnosis, followed by uterine cancer. Fifty participants (55.6%) had previously undergone abdominal surgery, and 47 (52.2%) were found to have adhesions during surgery. The duration of the operation and the amount of estimated blood loss in the two groups were similar (Table 1). Two participants in the control group experienced intraoperative bladder injury and excessive blood loss. All participants reported no smoking history.

Table 2 shows the outcomes of this study. Consumption of *Cassia alata Linn* early in the postoperative period significantly reduced time of first passage of flatus (MD -8.5 h; 95% CI -3.7, -13.4 h) and time to first defecation (MD -19.8 h; 95% CI -11.2, -28.5 h). No women in the *Cassia alata Linn* group experienced ileus symptoms that required additional treatment, compared to the 8.9% of the controls. There were no differences in terms of time to toleration of solid food or length of hospital stay between the two comparison groups. There were no clinically important changes in the findings after adjustment for factors that could potentially affect outcomes, including the type of operation, types of anesthesia, and the presence of adhesion during surgery.

Consumption of *Cassia alata Linn* infusion was reported to be well-tolerated by all patients, and no intervention-related adverse events were observed.

4. Discussion

The results of this study demonstrated that drinking *Cassia alata Linn* infusion hastened the recovery of gastrointestinal function by reducing the time to first passage of flatus and time to the first defecation compared with controls. Furthermore, *Cassia alata Linn* intake during the early postoperative period was found to be safe, as no intervention-

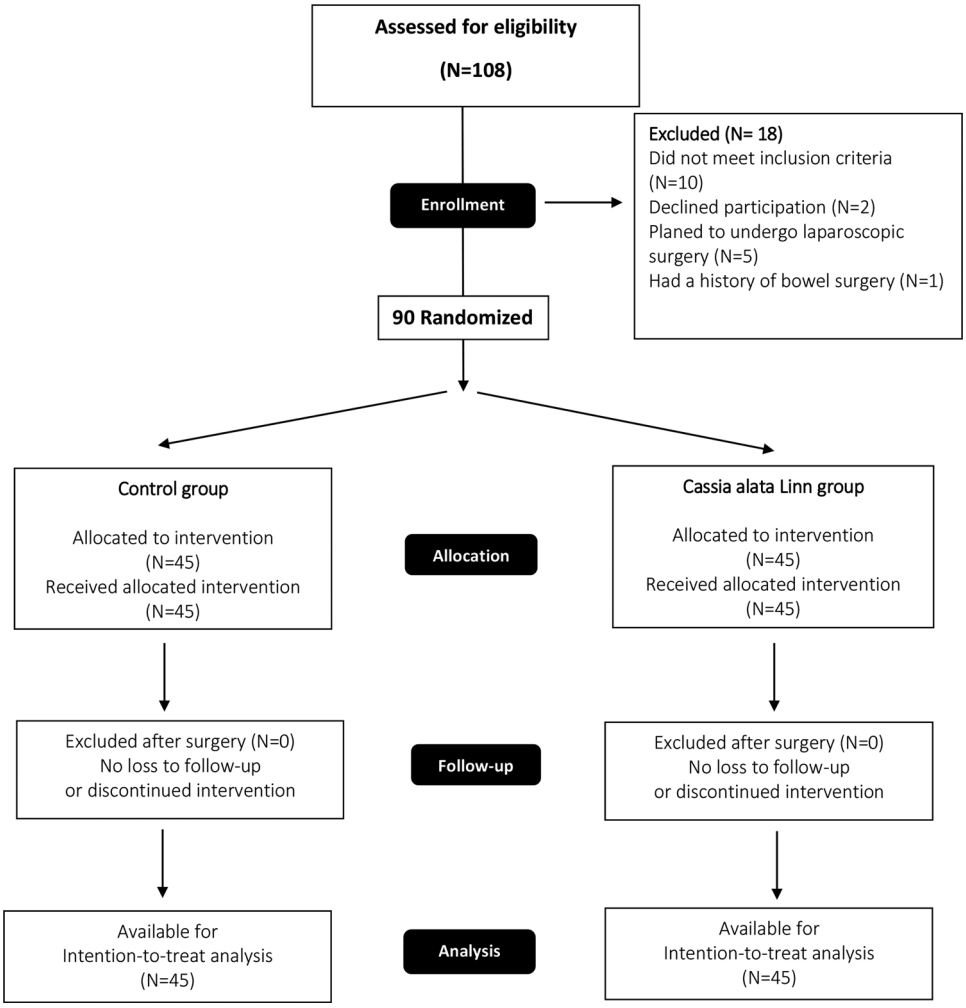

Fig. 1. xxx.

Table 1
Participants' baseline characteristics and intraoperative findings.

Characteristics	Total (n = 90)	*Cassia alata group* (n = 45)	Control group (n = 45)
Age (year), mean (SD)	54.6 (13.9)	55 (10.9)	54.2 (13.9)
BMI (kg/m2), median (IQR)	23.7 (21.2–28.0)	22.8 (20.8–26.7)	24.4 (21.9–29.3)
Gravida, median (IQR)	2 (1–3)	2(1–3)	2 (1–3)
Underlying diabetes	16 (17.8)	5 (11.1)	11 (24.4)
Underlying hypertension	30 (33.3)	13 (28.9)	17 (37.8)
Type of cancer			
- Cervical cancer	8 (8.9)	4 (8.9)	4 (8.9)
- Ovarian cancer	44 (48.9)	22 (48.9)	22 (48.9)
- Uterine cancer	38 (38.9)	19 (37.8)	19 (40.0)
Previous abdominal surgery	50 (55.6)	24 (53.3)	26 (57.8)
Mode of anesthesia			
- Neuraxial anesthesia	8 (8.9)	2 (4.4)	6 (13.3)
- General anesthesia	19 (21.1)	8 (17.8)	11 (24.4)
- Combined technique	63 (70.0)	35 (77.8)	28 (62.2)
Surgical procedure			
- Hysterectomy	86 (95.6)	45 (100.0)	41 (91.1)
- Retroperitoneal lymphadenectomy	36 (40.0)	22 (48.9)	14 (31.1)
Use of pelvic drains	11 (12.2)	5 (11.1)	6 (13.3)
Presence of adhesion during operation	47 (52.2)	21 (46.7)	26 (57.8)
Operation time (hours), mean (SD)	2.0 (0.6)	2.1 (0.6)	1.9 (0.5)
Estimate blood loss (ml), median (IQR)	100 (50–200)	100 (50–200)	100 (50–200)
Intraoperative complications	2 (2.2)	0 (0.0)	2 (4.4)
Overall costs (Bath), median (IQR)	35,271 (32,328–41,993)	35,641 (32,328– 41,168)	35,217 (33,106– 42,120)

Data are present as numbers (percentages) unless stated otherwise.
SD, standard deviation; IQR, interquartile range; BMI, body mass index.

Table 2
Study outcomes.

Outcomes	Total (n = 90)	*Cassia alata Linn* group (n = 45)	Control group (n = 45)	Effect measures (95% CI)	Adjusted effect measure[a] (95% CI)
Time to first passage of flatus (hours), mean (SD)	30.7 (12.3)	26.4 (1.1)	34.9 (2.2)	MD −8.53 (−3.69, −13.38)	MD -9.08 (−3.89, −14.28)
Time to first defecation (hours), mean (SD)	56.8 (22.8)	46.9(2.1)	66.7 (3.8)	MD −19.83 (−11.18, −28.48)	MD −17.49 (−8.29, −26.70)
Number of audible bowel movements at 12 hours, mean (SD)[b]	12.2 (4.1)	13.0 (4.3)	11.3 (3.9)	MD 1.73 (0.03, 3.44)	MD 1.70 (−0.15, 3.55)
Number of audible bowel movements at 24 hours, mean (SD)[b]	11.6 (5.3)	12.4 (6.0)	10.7 (4.3)	MD 1.76 (−0.43, 3.94)	MD 1.84 (−0.53, 4.20)
Time to toleration of solid food (hours), mean (SD)	20.2 (4.4)	20.0 (4.3)	20.3 (4.6)	MD 0.26 (−2.13, 1.61)	MD 0.03 (−1.95, 2.02)
Ileus symptoms requiring additional treatment	4 (4.4)	0 (0)	4 (8.9)	OR 0.10 (0.01, 1.94)	OR 0.19 (0.01, 3.91)
Postoperative complications[c]	6 (6.7)	3 (3.7)	3 (6.7)	OR 1.00 (0.21, 4.67)	OR 0.83 (0.16, 4.30)
Length of hospital stay (days), mean (SD)	8.0 (4.2)	7.9 (4.8)	8.1 (3.6)	MD −0.56 (−1.93, 1.62)	MD −0.20 (−2.11, 1.72)

CI, confidence interval; SD, standard deviation; MD, mean difference; OR, odds ratio.

[a] Adjusted by types of surgical procedure, presence of adhesion during operation, and mode of anesthesia.

[b] Measured within 2 min using stethoscope.

[c] Including wound complications (4), infective diarrhea (1), and neurogenic bladder (1).

related adverse events were observed.

Postoperative ileus remains a focus of concern for postoperative care of patients undergoing abdominal surgery. Currently accepted interventions for enhancing the recovery of gastrointestinal function after abdominal surgery include chewing gum and postoperative coffee consumption.[4,12] A Cochrane review conducted by Short et al.[12] noted that chewing gum during the early postoperative period can improve postoperative gastrointestinal function recovery among patients undergoing abdominal surgery by shortening the time to first passage of flatus (−10.4 h; 95% CI: −11.9, −8.9), time to first bowel movement (−12.7 h; 95% CI, −14.5, −10.9), and time to first bowel sound (−5.0 h; 95% CI, −6.4, −3.7). Similarly, a systematic review conducted by Eamudomkarn et al.[4] noted that postoperative coffee consumption facilitated the recovery of gastrointestinal function after abdominal surgery by reducing time to first defecation (−10.0 h; 95% CI, −17.0, −3.0), time to first flatus (−7.1 h; 95% CI, −11.0, −3.3), time to first bowel sound (−4.2 h; 95% CI, −7.9, −0.5), and time to tolerance of solid food (−15.6 h; 95% CI, −22.8, −8.3). Both systematic reviews consistently observed that the effectiveness of these interventions increased with the complexity of the operation.[4,12]

A delay in the return of gastrointestinal function with the passage of flatus and feces is common and can be a factor contributing to delayed recovery and discharge in patients who undergo surgery for gynecologic cancer because of the extensive nature of such operations.[13] Chewing gum and coffee intake during the early postoperative period have been reported to be effective interventions to alleviate postoperative ileus among women with gynecologic cancer undergoing tumor staging or cytoreduction.[11,13] In a study by Güngördük et al.,[11] mean time to flatus (30.2 versus 40.2 h), mean time to defecation (43.1 versus 58.5 h), and mean time to the ability to tolerate food (3.4 versus 4.7 days) were significantly shorter in gynecologic cancer patients who consumed coffee compared with controls. In addition, another study found that gynecologic cancer patients assigned to a gum-chewing group experienced shorter mean time to first flatus (43.6 versus 34.0 h) and mean time to first defecation (62.5 versus 49.6 h) compared to those given no intervention.[13]

In this study, women assigned to drink *Cassia alata Linn* infusion experienced shorter mean time to first passage of flatus and time to first defecation compared to the control subjects. These benefits remained unchanged after adjustment for variables that could have potentially affected these outcomes (Table 2). Another interesting finding was that the postoperative consumption of *Cassia alata Linn* tended to decrease postoperative ileus. Approximately 9% of women in the control group experienced ileus symptoms that required additional treatment compared to none in the *Cassia alata Linn* group (Table 2). These findings, therefore, suggest that postoperative consumption of *Cassia alata Linn* is a promising intervention that can promote early recovery of gastrointestinal function following extensive surgery for gynecologic cancer.

Common side effects of *Cassia alata Linn* consumption are nausea, abdominal pain, and diarrhea.[9] These side effects are mostly mild and self-limiting.[9] In the present study, drinking an infusion tea made from *Cassia alata Linn* appeared to be safe, as no intervention-related side effects were observed. In addition, the postoperative consumption of *Cassia alata Linn* infusion was reported to be well-tolerated. This suggests that the postoperative consumption of *Cassia alata Linn* infusion is feasible as an adjunct to routine postoperative care.

A relatively small sample size is a limitation of this study that made it difficult to reach a meaningful conclusion regarding the impact of the intervention on some clinically relevant outcomes (i.e., time to toleration of solid food, severe ileus symptoms, and length of hospital stay).

To our knowledge, this is the first randomized trial in the English-language literature to investigate the effects of *Cassia alata Linn* consumption in the early period following surgery. Although the lower incidence of severe postoperative ileus among women given *Cassia alata Linn* compared to the controls is worthy of consideration, a large-scale study is required to confirm this finding.

In conclusion, postoperative consumption of *Cassia alata Linn* hastened the recovery of gastrointestinal function after laparotomy for surgical staging or tumor cytoreduction among women with gynecologic cancer by reducing the time to first passage of flatus and time to the first defecation. Additionally, consumption of *Cassia alata Linn* infusion during the early postoperative period appeared to be safe, making it a feasible alternative to gum-chewing or coffee consumption in the postoperative care of gynecologic cancer patients.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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