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Original Research Article

Effect of *Launaea taraxacifolia* on Pregnancy Outcome, its Safety Profile and Mechanism(s) of Alleviating Labour Pain in Gravid Rats

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Abstract

Purpose: *Launaea taraxacifolia* (LT) is traditionally utilised by pregnant women to ease labour. This study evaluated LT's effects on pregnancy outcomes, its safety profile, and the mechanism by which it alleviates labour pain.

Methods: Whole plants of LT were extracted by maceration in distilled water. Pregnant rats were assigned to four groups and treated as follows: control (distilled water, 5 mL/kg/day); 25, 50, and 100 mg/kg/day LT, respectively, from gestational day (GD) 14 to GD 20. On GD 21, pups were delivered via caesarean section, and pregnancy outcome parameters were assessed. Blood samples, amniotic fluid, umbilical cord, placenta, and maternal organs were analysed. The active constituents in LT were identified using High-performance liquid chromatography (HPLC) analysis.

Results: No significant differences were observed in pregnancy outcomes, including the weights of dams, pups, and placenta; litter size; crump-rump length; and head circumference. Biochemical analyses indicated a reduction in sodium and chloride ions in the 100 mg/kg LT dose group and an increase in alkaline phosphatase in the 50 and 100 mg/kg LT groups. Estradiol levels decreased across all treated groups; however, prostaglandin E2 concentrations in both the amniotic fluid and umbilical cord samples remained unchanged, while prostaglandin F2α increased significantly in the amniotic fluid of the treated groups. Major active components in LT include cyanogenic glycosides, phytate, epihendrine, steroids, flavan-3-ols, anthocyanins, and naringin.

Conclusion: LT had no adverse effect on pregnancy outcomes, and its mechanisms for alleviating labour pain and facilitating labour may be attributed to its effects on estradiol and prostaglandin F2α.

Keywords: *Launaea taraxacifolia,* Pregnancy, Labour pain, Prostaglandin E2, Prostaglandin F2α, Estradiol.

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INTRODUCTION

The use of medicinal plants to induce labour, alleviate labour pain, facilitate delivery, manage retained placenta, and prevent excessive postpartum bleeding is well documented.[1-4] A systematic review and meta-analysis by Zamawe et al.[5] concluded that herbal remedies can be effective for labour induction but highlighted the lack of comprehensive safety data. Concerns about the safety of herbal use in pregnancy stem from both the pharmacological properties of the plants and the risk of interactions with conventional medications.[6] Studies indicate that a significant proportion of pregnant women use herbal medicines without consulting healthcare professionals,[7-8], and up to 39% may consume herbs that are potentially harmful or lack established safety profiles.[9] The current paucity of clinical data on herbal use during pregnancy underscores the need for caution.[10]

Labour pain is widely recognised as one of the most intense forms of pain experienced by women, and its effective management is a cornerstone of modern obstetric care.[11] The degree of pain relief achieved during labour significantly influences maternal satisfaction and may have lasting emotional and psychological consequences.[12,13] Associations have been reported between labour pain and postpartum psychiatric disorders.[14-16] Non-pharmacological interventions, including complementary and alternative medicine, are now widely utilised, with a recent study noting that 73% of women globally use at least one such method during labour.[11] One such medicinal plant used to alleviate pain during labour and facilitate childbirth is *Launaea taraxacifolia* (LT).

Launaea taraxacifolia (Willd.) Amin ex C. Jeffrey, verified via World Flora Online on 25 February 2025, is commonly known as wild lettuce or African lettuce and is locally referred to as Noomen barewa (Hausa) or Yanrin (Yoruba). This species, a member of the Asteraceae family, is indigenous to tropical Africa, where it is cultivated as a leafy vegetable and consumed raw or cooked in soups and sauces.[17] It also grows wild in West Africa (notably Nigeria, Ghana, Senegal, and Benin), East Africa (such as Ethiopia and Tanzania), and parts of Southern Africa.[18,19] Beyond its nutritional role, *Launaea taraxacifolia* has a long history of use in African traditional medicine. It is used to manage conditions such as conjunctivitis, yaws, measles, and diabetes mellitus.[17] Previous studies have shown that the plant possesses numerous pharmacological activities, including antioxidant, anti-inflammatory, hepatoprotective, neuroprotective, anticancer, antimalarial, antibacterial, cardioprotective, and DNA-protective activities, attributed to its rich phytochemical content, including flavonoids, tannins, and alkaloids.[18] Ethnobotanical evidence from Sokoto, Nigeria, indicates that the decoction from the whole plant of *Launaea taraxacifolia* is traditionally used by pregnant women during the last trimester to ease delivery, reduce labour pain, and improve foetal outcomes.[20] Previous research has demonstrated its uterotonic activity in isolated uteri of pregnant rats,[20] and its methanol extract has been shown to influence pregnancy outcomes and certain biochemical parameters in rat offspring.[21]

Despite the widespread use of medicinal plants in pregnancy, the mechanisms underlying their effects remain poorly understood. The role of maternal steroid hormones in human parturition is a subject of ongoing debate, with conflicting reports regarding the significance of progesterone and estrogen fluctuations at term.[22-24] Oxytocin, a key hormone in parturition, promotes the synthesis of prostaglandins, notably prostaglandin E2 (PGE_2) and prostaglandin F2α (PGF2α), which are crucial for cervical ripening and uterine contractions.[25,26] Elevated estrogen levels at term further enhance oxytocin receptor sensitivity, facilitating effective labour.[22,27] This study aims to investigate the effects of *Launaea taraxacifolia* on pregnancy outcomes, assess its safety profile, and elucidate potential mechanisms by which it may alleviate labour pain and facilitate childbirth in rats.

MATERIALS AND METHODS

Drugs, Chemicals, Solvents and Equipment

Diethyl ether and formalin were obtained from Sigma-Aldrich Chemical Co. (Darmstadt, Germany). Normal saline (Unique Pharmaceutical Limited, Nigeria) was obtained from a local pharmacy. Phosphate-buffered saline was obtained from Loba Chemie Pvt. Ltd., India, and glycerol from Research Products International, USA. The equipment includes a haematology autoanalyser (Shenzhen Mindray Bio-Medical Electronics Co. Ltd., China; Model: BC-20), a microplate reader (Rayto Life Analytical Sciences Co. Ltd., China; Model: RT 21OOC), a centrifuge (LifeTek Medical, England; Model: 80-24), a hot water bath (Surgifriend Medicals, England; Model: SM801A), a microscope (Olympus, Japan; Model: CX23), and a weighing balance (Mettler Toledo, USA; Model: PL203).

Collection, Identification and Extraction of Plant Material

The whole plant of LT was collected from the Talata Mafara area in Zamfara State. The plant was

identified and authenticated at the herbarium of the Department of Biological Sciences, Usmanu Danfodiyo University, Sokoto, where a herbarium specimen (voucher number UDUH/ANS/0010) was deposited. The whole plant material was air-dried in the shade until it reached a constant weight, then ground into a fine powder using a mortar and pestle. Two hundred and fifty grams (250 g) of the dried plant powder were extracted by maceration with 2 litres of distilled water over 24 hours. The extract was filtered through Whatman's filter paper, and the filtrate was evaporated to dryness in a water bath at 45 °C. The percentage yield of the plant material was calculated using the formula provided below:

$$\%\text{Yield} = \frac{(\text{Weight of crude extract})(\text{g})}{\text{Weight of the powdered plant material(g)}} \text{ x } 100\%$$

Experimental Animals

Twenty-five female and ten male Sprague-Dawley rats, aged 10-12 weeks and weighing 165-184 g, were obtained and housed in the animal house facility of the Department of Pharmacology and Toxicology at Usmanu Danfodiyo University, Sokoto. The animals were kept under standard husbandry conditions with a natural photoperiod and humidity, and at a temperature of 26 ± 2 °C, and had free access to commercial chow (Chikun®, Crown Flour Mill Ltd, Nigeria) and drinking water. The care and handling of the animals were in accordance with the institution's guidelines for the use of animals in research, with approval number NHREC/UDU-HREC/25/06/2023-PGM12.

Experimental Design

Female rats in proestrus were mated overnight at a ratio of two females to one male, and vaginal smears were taken (using a flexible plastic pipette and normal saline) following overnight mating. The presence of sperm cells or a vaginal plug was designated as gestational day (GD) 1, and the animals were then kept in separate cages. Sixteen of the twenty- five rats were confirmed pregnant and on GD 14 were allotted to four groups of four animals each and treated thus: control (distilled water 5 mL/kg/day), low-dose LT group (25 mg/kg/day), medium-dose LT group (50 mg/kg/day) and high-dose LT group (100 mg/kg/day) until GD 20. The dosage regimen was based on a previous study reporting adverse effects in rat pups at LT doses exceeding 125 mg/kg.[21] This treatment period, starting from GD 14 through to GD 20, was designed to mimic the ethnobotanical use of the plant, which usually commences at the end of the second trimester; since GD days 7, 14 and 21 represent the end of the first, second and third trimesters, respectively, in rats.[28]

Sample Collection

On GD 21, the animals were weighed, anaesthetised with diethyl ether, and blood samples were collected via cardiac puncture for haematological, biochemical, and hormonal assays. A laparotomy was then performed to expose the uterine horns. The foetal sacs were gently opened, and amniotic fluid was collected with a sterile 5 mL syringe and transferred to a 2 mL cryovial. The umbilical cord was carefully excised, rinsed in ice-cold phosphate-buffered saline (0.01 M), and placed in a 2 mL cryovial containing 20% glycerol. Both samples were immediately transferred to a -80 °C freezer. The number of pups and their respective placentas were counted, weighed, and examined for morphological abnormalities. The crown-rump length and head circumference of the pups were measured using a ruler and string. The hearts, kidneys, and livers of the pregnant dams were rapidly harvested and placed alongside the placentas in 10% buffered formalin for histological analysis.

Biochemical Assays

Serum for liver and kidney biochemical assays was obtained from blood samples after centrifugation at 4000 rpm for 5 min. Liver parameters, namely aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein, albumin, total bilirubin and direct bilirubin, and kidney parameters, namely creatinine, urea and electrolytes (sodium, potassium, chloride and bicarbonate), were estimated using standard laboratory kits (Randox Laboratories Limited, United Kingdom, and Teco Diagnostics, USA), following the manufacturers' instructions.

Haematological Analysis

Haematological analysis of the blood samples was performed using a haematology autoanalyser. Parameters evaluated include white blood cell (WBC), red blood cell (RBC), lymphocyte, granulocyte, haemoglobin concentrations, hematocrit (HCT), mean cell volume (MCV), mean cell haemoglobin (MCH), Mean cell haemoglobin concentration (MCHC), red cell distribution width-coefficient variation (RDW-CV), red cell distribution width-standard deviation (RDW-SD), platelet count, mean platelet volume (MPV), platelet distribution width (PDW), platelet hematocrit, and platelet large cell.

Estradiol and Progesterone Assays

Serum obtained from the pregnant dams was analysed for estradiol and progesterone concentration using the AccuBind ELISA

microwell kits (Monobind Inc., USA. Lot No EIA-49K1L4) following the manufacturer's instructions.

Prostaglandin Assays

The umbilical cord and amniotic fluid samples were taken from the -80 °C freezer and allowed to thaw. The umbilical cords were then removed from the glycerol preservative, blotted with absorbent paper, and placed in sterile microcentrifuge tubes. The samples were mixed with 1 ml of PBS for washing, then centrifuged at 500 rpm for 3 minutes. Afterwards, the samples were blotted with absorbent paper and transferred to pre-cooled 5 ml glass homogenisers for protein extraction. Total protein lysate was obtained from the umbilical tissues using a Tissue protein extraction reagent with a protease inhibitor cocktail (Elabscience® Texas, USA, Catalogue No: E-BC-E002), following the manufacturer's protocol. Immunoassays for PGE2 and PGF2α content in the total protein extracted from the umbilical cord and amniotic fluid samples were performed using the Rat Prostaglandin E2 and Prostaglandin F2α enzyme immunoassay kits (PARS BIOCHEM, Nanjing Pars Biochem CO., Ltd, Nanjing, China, Catalogue No: PRS-30539Ra and PRS-30541Ra, respectively), according to the manufacturer's instructions.

Histological Analysis

All fixed tissues, including the heart, liver, kidney, and placenta, were dehydrated in alcohol, cleared in xylene, and embedded in paraffin wax melted at 60 °C. Serial sections (5 µm thick) were mounted on 3-aminopropyl triethylsilane-coated slides and dried at 37 °C for 24 hours. The sections were deparaffinised, rehydrated, stained with Mayer's haematoxylin and eosin, and dried. Slides were examined under a light microscope, and photomicrographs were captured at 200× magnification.

High-performance liquid chromatography analysis (HPLC)

The active constituents present in the aqueous extract of *Launaea taraxacifolia* were identified through HPLC analysis using Agilent 1100 dual binary pumps, an HP CTO-10AS column oven, and an HP Prominence SPD-20A UV/Vis detector. Briefly, 0.2g of the sample was weighed into a test tube, and 15 mL of ethanol and 10 mL of 50% m/v potassium hydroxide were added; then the mixture was heated in a water bath at 60 °C for 3 hours. Afterwards, it was transferred to a separatory funnel and washed with 20 mL of ethanol, 10 mL of cold water, 10 mL of hot water, and 3 mL of hexane, all of which were transferred to the funnel. This extract was combined and washed three times with 10 mL of a 10% (v/v) ethanol aqueous solution, and the ethanol was then evaporated. The sample was solubilised in 1000 µL of pyridine, of which 200 µL was transferred to a vial for HPLC analysis. The analysis was performed using a C-12 normal-phase column (Phenomenex, Gemini 5 µ, 200 mm length × 4.8 mm internal diameter). The mobile phase consisted of acetic acid-acidified deionised water (pH 2.8) as solvent A and acetonitrile as solvent B at a flow rate of 0.8 mL/min. The column was equilibrated with 5% solvent B for 20 minutes after each sample injection. The column temperature was set to 38 °C, and the injection volume was 20 µL. The wavelength was set to 280 nm for phytochemical detection. Phytochemicals were identified and quantified by comparing retention times and peak areas with those of pure standard compounds, using the external standard method to construct a calibration curve. Gradient elution was executed as follows: 0-5 min, 5-9% solvent B; 5-15 min, 9% solvent B; 15-22 min, 9-11% solvent B; 22-38 min, 11-18% solvent B; 38-43 min, 18-23% solvent B; 43-44 min, 23-90% solvent B; 44-45 min, 90-80% solvent B; 45-55 min.

Statistical Analysis

Data were expressed as mean ± standard error of the mean (SEM), and statistical analyses were performed using GraphPad Prism software, version 8.0 (GraphPad Software, Boston, MA, USA). Comparisons were conducted using one-way analysis of variance (ANOVA) followed by Dunnett's post hoc test. *P*-values less than 0.05 were considered significant.

RESULTS AND DISCUSSIONS

Effect of aqueous extract of *Launaea taraxacifolia* on Gross morphology and pregnancy outcome parameters

There were neither birth abnormalities on gross examination of the pups nor stillbirths observed in the control and all treated groups. Furthermore, we observed no statistically significant differences in the evaluated pregnancy outcome parameters, including litter size, placental weight, head circumference, crown-rump length of the pups at parturition, and weight gain of the dams, between the control group and all treated groups. However, pup birth weight increased in a non-dose-dependent manner across all test groups compared with the control, though this difference was not statistically significant (Table 1).

Table 1: Effect of aqueous extract of *Launaea taraxacifolia* on the pregnancy outcome in rats

Parameters	Control (5mL/kg DW)	25 mg/kg LT	50 mg/kg LT	100 mg/kg LT
Weight gain in dams (g)	52.68 ± 14.93	58.33 ± 8.84	50.48 ± 11.64	43.35 ± 11.65
Weight of placenta (g)	0.43 ± 0.04	0.45 ± 0.07	0.37 ± 0.02	0.42 ± 0.02
Weight of pup (g)	2.97 ± 0.36	3.55 ± 0.26	3.83 ± 0.10	3.61 ± 0.61
Crump-rump length (cm)	3.92 ± 0.03	3.62 ± 0.07	3.79 ± 0.17	3.72 ± 0.35
Head circumference (cm)	3.96 ± 0.01	3.59 ± 0.09	3.64 ± 0.05	3.45 ± 0.31
Litter size	9.25 ± 1.25	8.00 ± 0.00	9.25 ± 1.25	10.50 ± 0.50

Data are expressed as mean ± standard error of mean. DW: Distilled water, LT: Aqueous extract of *Launaea taraxacifolia*

Although we observed no significant difference in pregnancy outcome parameters, including litter size, placental weight, head circumference, and crown-rump length of the pups at parturition, as well as in dam weight gain, the birth weight tended to be higher in the treated groups. This result is similar to a previous study, in which the methanol extract of LT at doses of 125 and 250 mg/kg significantly increased birth weight and weight at postnatal day 21.[21] Studies have shown that hormone levels influence embryonic growth. Placental cells are believed to be the primary source of hormones required for embryonic growth and development.[29] The results of this study suggest that LT may affect growth hormone levels in pregnant rats. Since birth length, birth weight, and litter size are significant predictors of adult stature,[30] it can be inferred that LT may influence postnatal body mass index even at the lower dose levels reported in this study. The absence of histopathological alterations in placental tissues across groups indicates that nutrient transfer to the pups in utero was not compromised. Although Adebisi et al.[21] reported a significant decrease in litter size at 250 mg/kg, with all foetuses aborted at 500 mg/kg. The results show that the LT extract does not adversely affect litter size at the lower doses used.

Effect of aqueous extract of *Launaea taraxacifolia* on kidney and liver function, haematological parameters and Histology of pregnant dams.

Biochemical analysis of the kidneys of pregnant dams showed a statistically significant decrease in sodium and chloride ion concentrations in the group treated with 100 mg/kg LT (Table 2).

Table 2: Effect of aqueous extract of *Launaea taraxacifolia* on kidney function in pregnant rats

Parameters	Control (5 mL/kg DW)	25 mg/kg LT	50 mg/kg LT	100 mg/kg LT
Na (mmol/L)	139.00 ± 1.08	139.00 ± 0.58	137.00 ± 0.91	132.80 ± 2.35*
K (mmol/L)	5.13 ± 0.13	5.03 ± 0.22	4.85 ± 0.53	5.78 ± 1.24
Cl (mmol/L)	95.50 ± 1.19	94.00 ± 0.58	92.50 ± 0.65	91.20 ± 1.43*
HCO3 (mmol/L)	31.50 ± 0.50	28.33 ± 2.60	27.50 ± 1.26	27.60 ± 1.36
Urea (mmol/L)	7.93 ± 0.51	7.53 ± 1.07	6.90 ± 0.39	7.24 ± 0.54
Cr (mg/dL)	0.45 ± 0.05	0.53 ± 0.07	0.58 ± 0.03	0.62 ± 0.09

Data are expressed as mean ± standard error of the mean. DW: Distilled water, LT: Aqueous extract of *Launaea taraxacifolia*, Na: Sodium, K: Potassium, Cl: Chloride, HCO3: Bicarbonate, Cr: Creatinine, *p < 0.05 compared to control.

In the liver function test, alkaline phosphatase levels increased significantly in the groups that received 50 and 100 mg/kg LT compared with the control group. All other parameters did not differ significantly from the control group (Table 3).

Table 3: Effect of aqueous extract of *Launaea taraxacifolia* on the liver function of pregnant rats

Parameters	Control (5 mL/kg DW)	25 mg/kg LT	50 mg/kg LT	100 mg/kg LT
AST (IU/L)	116.10 ± 30.11	183.80 ± 51.63	203.10±44.66	220.60 ± 27.52
ALT (IU/L)	66.43 ± 10.14	94.80 ± 20.44	92.98 ± 13.99	77.90 ± 6.28
ALP (IU/L)	202.60 ± 14.48	316.20 ± 45.10	359.50 ± 39.25*	336.60 ± 36.61*
TP (g/L)	4.85 ± 0.69	4.60 ± 0.25	4.90 ± 0.26	6.04 ± 0.49
ALB (g/L)	2.83 ± 0.21	2.63 ± 0.15	2.63 ± 0.09	3.10 ± 0.21

TB (mg/dL)	0.64 ± 0.11	0.75 ± 0.03	0.79 ± 0.12	0.59 ± 0.06
DB (mg/dL)	0.15 ± 0.03	0.16 ± 0.04	0.29 ± 0.05	0.19 ± 0.03

Data are expressed as mean ± standard error of the mean. DW: Distilled water, LT: Aqueous extract of *Launaea taraxacifolia*, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, TP: Total protein, ALB: Albumin, TB: Total bilirubin, DB: Direct bilirubin, *p < 0.05 compared to control.

Histological analysis of the livers of pregnant dams revealed ballooning degeneration in hepatocytes in the treated groups compared with the control. The heart showed regular myocardial cells, while the kidney exhibited normal glomeruli and tubules with few eosinophilic collections. The placentas of the control and treated groups had regular proliferating trophoblastic tissues with degenerating glycogen cells. The photomicrographs of the liver, heart, and kidney of the pregnant dams and the placenta of the pups are presented in Figures 4, 5, 6, and 7, respectively. However, no significant differences were observed in any of the measured haematological parameters between the treated groups and the control (Table 4).

Table 4: Effect of aqueous extract of *Launaea taraxacifolia* on the haematological parameters in pregnant rats

Parameters	Control (5ml/kgDW)	25 mg/kgLT	50 mg/kgLT	100 mg/kgLT
WBC	9.40±0.81	9.53±2.86	24.80±13.78	21.56±8.86
Lymp	8.10±1.08	6.63±2.19	19.87±10.87	16.14±5.74
Mid	0.60±0.08	0.83±0.20	2.03±1.13	2.60±1.50
Gran	0.70±0.20	2.07±0.89	2.90±1.85	2.82±1.67
Lymph %	84.60±4.98	67.27±10.19	80.68±3.69	81.84±4.093
Mid %	7.10±1.68	10.37±3.68	8.35±1.30	8.52±2.39
Gran %	4.90±0.06	22.37±6.98	10.98±3.8	9.64±2.63
RBC	5.28±0.26	4.65±0.51	3.89±0.51	3.40±0.89
HGB	11.75±0.35	10.77±0.55	10.10±0.16	11.24±1.01
HCT	31.02±1.25	34.60±1.27	28.00±3.34	24.78±6.82
MCV	58.92±1.01	75.90±6.98	72.68±4.63	71.42±2.64
MCH	22.35±0.62	23.50±1.67	27.53±4.33	28.24±4.78
MCHC	291.95±84.47	311.90±13.53	378.75±53.13	399.70±70.48
RDW-CV	3.28±3.04	0.17±0.01	0.27±0.05	0.33±0.04
RDW-SD	41.48±7.34	42.57±0.67	65.06±15.71	75.92±8.85
PLT	636±49.72	315.67±68.17	747.75±136.18	343.26±97.33
MPV	7.05±0.44	7.60±0.90	8.32±0.55	8.02±0.45
PDW	12.78±1.99	15.13±0.28	15.57±0.25	15.42±0.34
PCT	4.16±0.29	2.29±0.29	6.20±1.23	3.41±0.72
P-LCR	1.19±1.06	0.14±0.04	0.21±0.05	0.18±0.03

Data are expressed as mean ± standard error of the mean. DW: Distilled water, LT: *Launaea taraxacifolia*, WBC: White Blood Cell, Lymp: Lymphocyte, Mid: Mid-sized cells, Gran: granulocyte, RBC: Red blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean cell volume, MCH: Mean cell hemoglobin, MCHC: Mean cell hemoglobin concentration, RDW-CV: Red cell distribution width-coefficient variation, RDW-SD: Red cell distribution width-standard deviation, PLT: Platelet count, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Platelet hematocrit, P-LCR: Platelet large cell ratio

Although the observed increase in liver alkaline phosphatase (ALP) levels at 50 and 100 mg/kg doses may indicate altered liver function, elevated ALP levels are also associated with bile duct obstruction, kidney disease, or bone disease.[31] Attendant elevations of other liver enzymes, such as gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT), indicate that the elevation of ALP is from a hepatic source.[32] However, histological findings of ballooning degeneration in hepatocytes suggest some cellular injury, though it may not be associated with significant impairment of hepatic function. Similarly, decreased sodium and chloride levels may reflect changes in renal filtration and electrolyte balance. Hypochloremia frequently appears along with hyponatremia,[33] and they could be associated with conditions such as congestive heart failure, renal and liver dysfunction.[34] The histological analysis of the heart, though, did not show any histopathological alterations; there were a few eosinophil collections in the kidneys. Contrary to our results, Kuatsienu et al.[35] and Diallo et al.[36] did not report any treatment-related abnormalities in biochemical parameters following 14- and 28-day treatments with the

extract of *Launaea taraxacifolia*, respectively. Furthermore, some previous studies have reported that *Launaea taraxacifolia* possesses antioxidant and hepatoprotective properties, mitigating oxidative stress in liver and kidney tissues.[18,37]

Effect of aqueous extract of *Launaea taraxacifolia* on serum concentrations of estradiol and progesterone in pregnant dams.

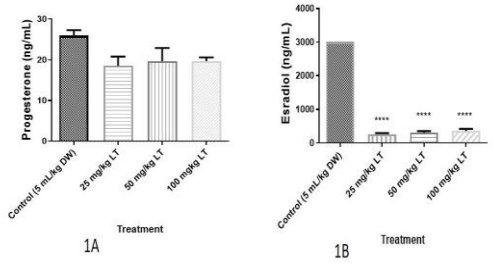


Figure 1: 1A and 1B represent the effect of aqueous extract of *Launaea taraxacifolia* on progesterone and estradiol concentration in pregnant rats, respectively. Data are presented as mean ± standard error of the mean. DW: Distilled water, LT: *Launaea taraxacifolia*. **** p< 0.0001

The hormonal assay results showed a non-dose-dependent reduction in progesterone levels across all treated groups. However, this was not statistically significant compared to the control (Figure 1A). However, estradiol levels decreased significantly and dose-dependently in the treated groups compared with the control group (Figure 1B). The purpose of this analysis was to investigate the mechanism by which *Launaea taraxacifolia* facilitates delivery. The observed decrease in estradiol levels suggests that *Launaea taraxacifolia* may selectively influence estrogenic activity during pregnancy. Estradiol, a primary form of estrogen, makes oxytocin receptors more sensitive to oxytocin.[22,27] Oxytocin, on the other hand, stimulates prostaglandin synthesis, which contributes to uterine contraction during labour.[26] This reduction in estradiol and the consequent effects on oxytocin receptor sensitivity and prostaglandin synthesis may be a probable mechanism underlying its claimed ability to alleviate labour pain. In addition, in most animal models, progesterone is the dominant hormone throughout pregnancy and decreases before labour onset.[22] In this study, a general trend of decreasing progesterone concentration was observed, though not significantly different on post hoc analysis. This decrease in progesterone is considered beneficial for initiating the cascade of events associated with labour.[23] Chauhan et al. (2024) have demonstrated that women who engages in regular exercise during pregnancy reported lower pain scores and less labour induction[38], and the proposed mechanism being related to metabolic and hormonal changes that increase uterine contractility.[39] Progesterone is one of the hormones that have been reported to reduce significantly in females following physical and flexibility exercise.[40]

Effect of *Launaea taraxacifolia* on Prostaglandin E2 and Prostaglandin F2α concentrations in the amniotic fluid and umbilical cord

Table 5: Effect of aqueous extract of *Launaea taraxacifolia* on Prostaglandin E2 concentration in the amniotic fluid and umbilical cord

Sample	Prostaglandin E2 concentration (ng/L)			
	Control (5mL/kg DW)	25 mg/kg LT	50 mg/kg LT	100 mg/kg LT
Amniotic fluid	4.26 ± 0.83	4.29 ± 0.96	4.59 ± 0.84	4.06 ± 0.16
Umbilical cord	4.56 ± 0.58	4.74 ± 0.85	4.85 ± 0.34	4.65 ± 0.50

Data are expressed as mean ± standard error of the mean. DW: Distilled water, LT: Aqueous extract of *Launaea taraxacifolia*.

The assay results for PGE2 concentration in amniotic fluid and umbilical cord showed no significant difference between the treated groups and the control (Table 5). The concentration of PGF2α, however, increased significantly in a non-dose-dependent manner in the amniotic fluids of all the treated groups compared to the control (Figure 2), while its concentration in the umbilical cords was below the detectable range.

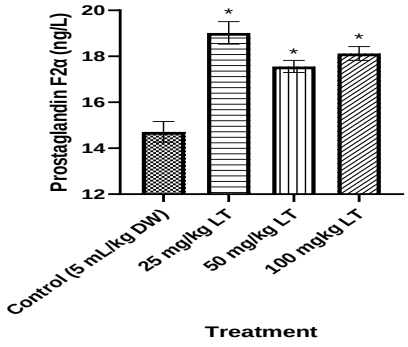


Figure 2: Effect of aqueous extract of *Launaea taraxacifolia* on Prostaglandin F2α concentration in the amniotic fluid. Data are expressed as mean ±

standard error of the mean. DW: Distilled water, LT: Aqueous extract of *Launaea taraxacifolia*, *p<0.001 compared to control.

This analysis aimed to further investigate the mechanism by which *Launaea taraxacifolia* facilitates delivery. PGE2 and PGF2α are the two most essential prostanoids associated with parturition. This has been demonstrated by their increased production during labour and by a delay in parturition achieved through inhibition of cyclooxygenases, the rate-limiting enzymes in prostaglandin synthesis.[41] Their role, mediated by G-protein-coupled receptors, includes contraction of the myometrium, cervical ripening, rupture of fetal membranes, and inflammation of uterine tissues.[42-44] PGE2 primarily ripens the cervix and promotes dilation, while PGF2α is mainly involved in uterine contraction, suggesting that PGE2 may be important in preparation for labour onset. At the same time, PGF2α may play a more significant role in expelling the fetus, i.e. labour accomplishment.[41] Though some previous studies have assayed these prostaglandins in maternal circulation,[45,46] PGE2 and PGF2α that enter the systemic circulation are known to be freely metabolised by 15-hydroxyl prostaglandin dehydrogenase. Hence, regarding their association with labour, it is more appropriate to assay their concentrations in amniotic fluid and other gestational tissues rather than in maternal serum.[41] Studies have reported that the umbilical cord is a source of prostaglandins, and PGE_2 and PGF2α are localised in amniotic cells covering the umbilical cord.[47] The results of this study show the presence of detectable levels of PGE_2 in both the umbilical cord and amniotic fluid. The lack of a significant difference in PGE_2 concentration between the control and treated groups indicates that the LT extract does not affect PGE_2 levels. Therefore, this hormone may not be responsible for the observed activity. The significant increase in PGF2α concentration in amniotic fluid, however, may suggest a probable mechanism by which *Launaea taraxacifolia* facilitates delivery. Previous studies have reported that in late gestation, before labour, the concentration of PGE_2 surpasses that of PGF2α by more than twofold, while PGF2α appears to exceed that of PGE_2 during labour.[45] Though the pups were delivered by cesarean section in this study, hence no labour, a 3- to 4-fold increase in the concentration of PGF2α compared to PGE_2 was also observed. Previous reports revealed an increase in amniotic fluid prostaglandin concentrations (up to 25-fold for PGF2α) before the onset of spontaneous labour at term in humans, suggesting an important role for prostaglandins in initiating human parturition.[48]

High-performance liquid chromatography analysis

The HPLC analysis of the crude aqueous extract of *Launaea taraxacifolia* revealed the presence of twenty-one (21) compounds. The major compounds include cyanogenic glycosides, phytate, epihendrine, steroids, flavan-3-ols, anthocyanins, and naringin. Table 6 presents the comprehensive list of compounds, and Figure 7 shows the chromatogram. The compounds present in this extract have been reported to have both beneficial and toxic effects.

Table 6: HPLC analysis of constituents of aqueous crude extract of *Launaea taraxacifolia*

Component	Retention	Area	Height	Concentration	Units	Class of compound
Proanthocyanin	0.110	561.7208	222.208	0.6320	ppm	Flavonoid
Lunamarin	0.183	3787.2370	124.959	4.4360	µg/ml	Quinolone alkaloid
Naringin	2.390	12468.8678	203.396	9.7670	µg/ml	Flavonoid
Cardiac glycoside	4.120	6439.0392	107.073	6.5929	µg/ml	Steroidal glycone
Flavan 3 ol	6.016	18505.8704	298.351	10.7499	ppm	Flavonoid
Anthocyanin	7.466	8168.2068	138.998	10.5080	µg/ml	Flavonoid
Ribalinidine	10.366	19378.1656	319.450	8.3097	µg/ml	Quinololine alkaloid
Naringenin	12.970	5983.7040	100.620	5.6891	µg/ml	Flavonoid
Spartein	15.460	4717.6830	79.750	6.3410	µg/ml	Quinolizidine alkaloid
Rutin	17.966	10773.685	181.880	6.6855	µg/ml	Flavonoid
Cyanogenic glycoside	20.313	12044.96560	203.087	16.1895	ppm	Nitrile
Flavonones	22.730	9214.8346	154.355	3.9515	ppm	Flavonoid
Steroids	25.650	9877.4402	163.611	12.7068	ppm	Steroid
Kaempferol	27.536	11128.3451	185.848	7.7066	µg/ml	Flavonoid
Epicatechin	29.860	5158.3293	87.501	7.7386	µg/g	Flavonoid
Phytate	32.996	14257.1034	233.200	15.9690	µg/ml	Organophosphate
Flavone	34.600	5611.0061	96.493	5.2228	µg/ml	Flavonoid
Oxalate	36.878	6421.6611	110.381	8.9423	µg/ml	Dicarboxylic acid
Resveratol	39.200	9871.3256	165.134	3.7505	ppm	Polyphenol

Sapogenin	42.276	3468.1816	57.444	5.6996	µg/ml	Steroid/Triterpene
Epihedrine	44.170	10568.1228	172.796	15.4081	µg/ml	Alkaloid

The presence of flavonoid subclasses, including flavan- 3- ol, flavone, flavonol, and flavanones, could be advantageous to the mother and the foetus as they have been reported to possess antioxidant, anticancer, anti- inflammatory, cardioprotective, antibacterial, antiviral, neuroprotective, and antidiabetic properties.[49,50] Previous studies suggest that consuming foods naturally rich in total flavonoids and anthocyanidins helps prevent gestational diabetes mellitus,[51-53] and that evidence supports the potential health benefits of flavonoid ingestion during pregnancy, especially in complicated cases.[54-58] Some other studies, however, have reported safety concerns regarding flavonoid consumption during pregnancy. These concerns include impaired foetal development, impaired absorption of other nutrients, and long-lasting effects, such as an increased risk of early-onset disease, particularly acute childhood leukaemia.[59] Steroids (e.g., corticosteroids), when administered in pregnancy, reduce complications associated with preterm birth by significantly enhancing foetal lung development and increasing the chances of survival, especially if the baby is delivered between 24 and 35 weeks of gestation,[60] and during the periviable period (22 to 26 weeks of gestation).[61] Cyanogenic glycosides, on the other hand, when broken down, release hydrogen cyanide, a toxic substance associated with health complications including acute toxicity,[62] chronic toxicity,[63] neurological disorders,[64 65] growth retardation,[66] and goitre.[67] Phytate and oxalate are antinutrients that can chelate and affect the absorption of calcium and other micronutrients, such as iron, zinc, copper, and magnesium, from the diet.[68,69]

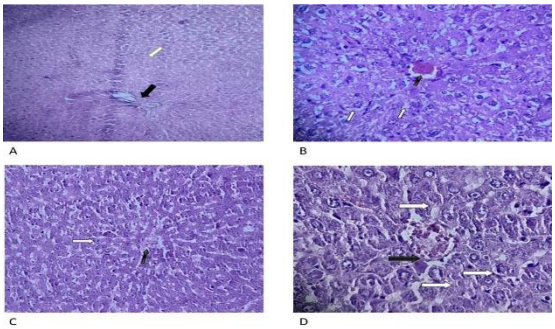


Figure 3: Effect of *Launaea taraxacifolia* on the histology of the Liver in pregnant rats
A (Control (DW 5mL/kg): Liver section showing regular hepatocytes (white arrow) and the portal triad (black arrow). H & E X 200
B (25 mg/kg LT): Liver section showing hepatocytes with ballooning degeneration (white arrow) and central vein (black arrow). H & E X 200.
C (50 mg/kg LT): Liver section showing hepatocytes with ballooning degeneration (white arrow) and central vein (black arrow). H & E X 200.
D (100 mg/kg LT): Liver section showing hepatocytes with ballooning degeneration (white arrow) and central vein (black arrow). H & E X 200.
LT: *Launaea taraxacifolia*, DW: Distilled water

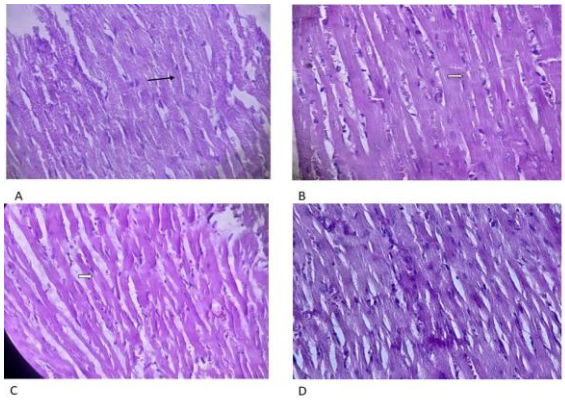


Figure 4: Heart section showing regular myocardial cells arranged in syncytium. H & E X 200. A: Control (DW 5mL/kg), B: 25 mg/kg LT, C: 50 mg/kg LT, D: 100 mg/kg LT, DW: Distilled water, LT: *Launaea taraxacifolia*

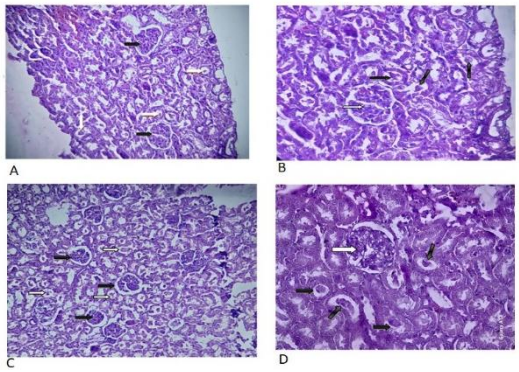


Figure 5: Kidney sections showing regular glomeruli (white arrow) and tubules with few eosinophilic collections within (black arrow). H & E X 200. A: Control (DW 5mL/kg), B: 25 mg/kg LT, C: 50 mg/kg LT, D: 100 mg/kg LT, DW: Distilled water, LT: *Launaea taraxacifolia*

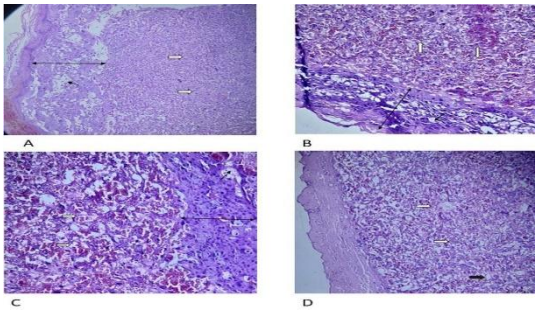


Figure 6: Placenta section showing regular proliferating trophoblastic tissues (white arrow) with degenerating glycogen cells (Black arrow) within the basal zone (black double arrowhead). H & E X 200. A: Control (DW 5mL/kg), B: 25 mg/kg LT, C: 50 mg/kg LT, D: 100 mg/kg LT, DW: Distilled water, LT: *Launaea taraxacifolia*

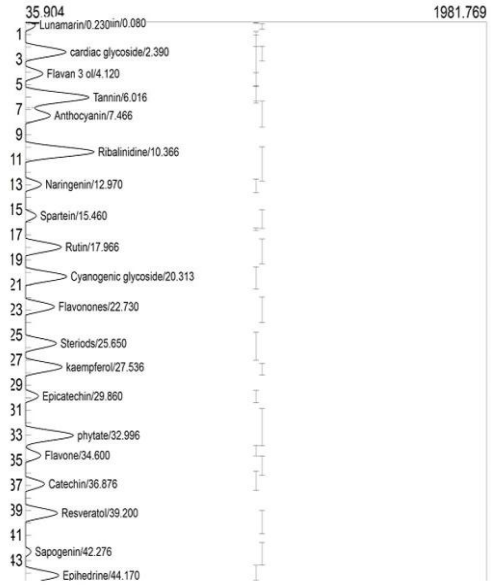


Figure 7: Chromatogram obtained from aqueous extract of *Launaea taraxacifolia* using high-performance liquid chromatography.

CONCLUSION

The extract of *Launaea taraxacifolia* did not adversely affect pregnancy outcomes, but alterations in certain kidney and liver biochemical parameters in the dams raise safety concerns. Additionally, analysis of its phytoconstituents revealed high levels of flavonoids, steroids, and alkaloids, all of which have been reported to have beneficial effects. On the other hand, the extract also contains high levels of antinutrients, such as phytate, oxalate, and cyanogenic glycosides, which may adversely affect the mother and the foetus. The observed decrease in serum estradiol concentration and the increase in PGF2α concentration in the amniotic fluid of the treated groups may be mechanisms by which it reduces labour pain and aids delivery.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS DECLARATION

The authors hereby declare that the works presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

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ABBREVIATIONS

ALP, Alkaline phosphatase; ALT, Alanine aminotransferase; ANOVA, Analysis of variance; AST, Aspartate aminotransferase; CL, Chlorine; Cr, Creatinine; DB, Direct bilirubin; DW, Distilled water; ELISA, Enzyme-linked Immunosorbent Assay; GD, Gestational day; GGT, gamma-glutamyltransferase; HCO3, Bicarbonate; HCT, Hematocrit; H&E, hematoxylin and eosin; HGB, Hemoglobin; HPLC, High-performance liquid chromatography; K, Potassium; LT, Launaea taraxacifolia; MCH, Mean cell hemoglobin; MCHC, Mean cell hemoglobin concentration; MCV, Mean cell volume; MPV, Mean platelet volume; Na, Sodium; PBS, Phosphate buffer saline; PDW, Platelet distribution width, PGE2, Prostaglandin E2; PGF2α, Prostaglandin F2α, P-LCR, Platelet large cell ratio; PLT, Platelet count; RBC, Red blood cell; RDW-CV, Red cell distribution width-coefficient variation; RDW-SD, Red cell distribution width-standard deviation; TB, Total bilirubin; TP, Total protein; SEM, Standard error of mean; WBC, White Blood Cell.

AUTHOR'S CONTRIBUTION

Iyabo Mobolawa Adebisi: Designed experiments, applied for research funding, analysed data, wrote the manuscript draft, and supervised the work. Isah Muhammad Baba, Chinenye Jane Ugwah

Oguejiofor, Abubakar Usman, Boniface Clement Gomo: Performed experiments and collected raw data. Umar Mohammed: Collected specimens and did pathological diagnosis. Oluranti Celestina Alebiosu: Performed experiments and did bioconstituent analysis. Ibrahim Malami: Performed experiments, did bioconstituent analysis and reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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